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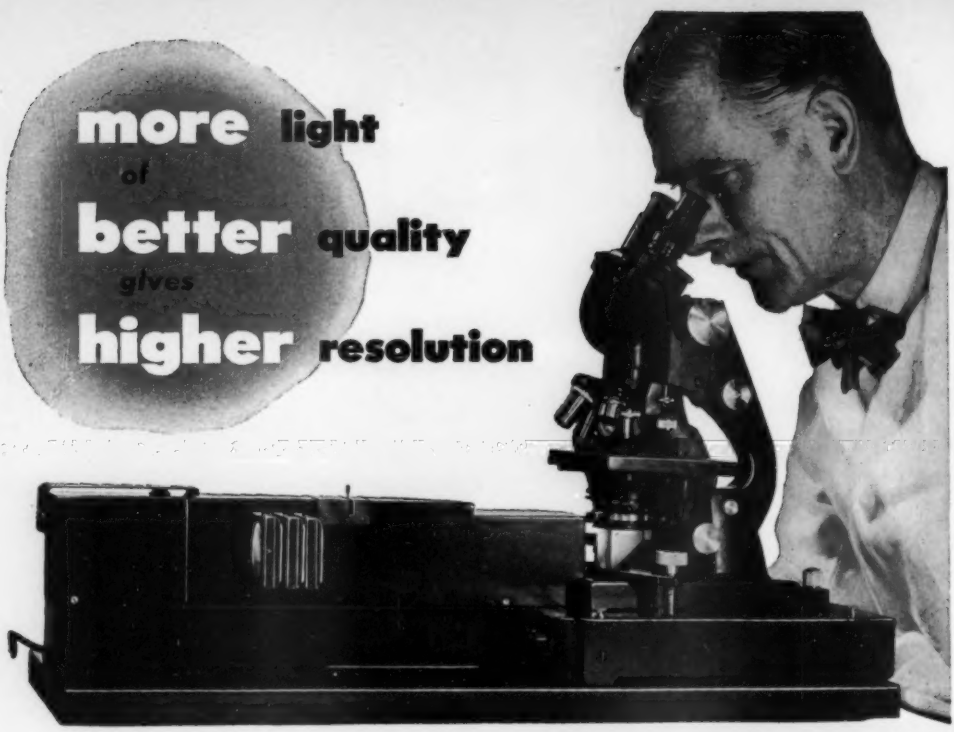

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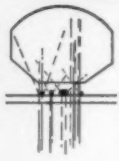

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P. V. CARDON
U. S. Department of Agriculture Graduate School

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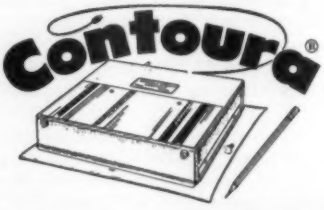

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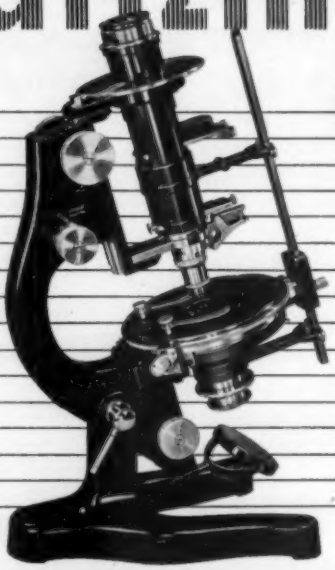

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Bioserological Methods of Human Classification

Nicolas Lahovary
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IN AUGUST 1950, in the columns of this periodical (SCIENCE, 112, 187 [1950]), William C. Boyd, who has done so much in the field of blood group research, commented somewhat critically on my own efforts toward a better interpretation of the bearing of serological investigations on the classification of the various human races and subraces. I will avail myself of this opportunity, not only to reply to his criticism, but at the same time to give the readers of SCIENCE a summary of my own methods and of their results.

Professor Boyd's principal point was that I "failed to realize that the characters by which we define races are independent of each other and we must not expect a classification by one character to agree with another very closely." This is sound common knowledge, and should I have been guilty of such an offense, I would have had to heap ashes on my head and wail in the Desert of Ignorance. The fact is, however, that this is not the case. On the contrary, I have myself shown, in the work mentioned by Boyd (pp. 90–91),[1] that his maps in the otherwise invaluable lists published in *Tabula Biologicae* in 1939 were bound to leave the reader puzzled, as they were based on the frequency of a *single* character, so that Finns and Arabs, Russians and Negroes, appeared related. After observing in others the pitfalls of such a concept, I would surely have taken care not to fall into the same error.

Nonetheless it would be a mistake to consider man as a genetic mosaic, a simple juxtaposition of various characters. All through nature there is an evident tendency toward a certain polygenism, toward genetic patterns that counterbalance the independence of the genes and impose harmony, where otherwise genetic independence might have led to anarchy. Thus, although the genes responsible for the various blood groups are quite different from those governing the color of the eyes or of the skin, the features of the face, the length of the limbs, etc., a certain physical pattern will be found associated, as a general rule, with a certain blood group pattern. Among Negroes of pure blood, for example, *all* the features will be characteristic of the black race, notwithstanding the independence of the genes responsible for each character. A specific physical pattern will entail, therefore, just as specific a blood pattern, notwithstanding the theoretical independence of the genes, not only for each blood system, but for each blood group of each system. There is a general specificity working for the unity of each organism and of each racial entity. The parallelism between the various gene systems may not be perfect, and with the mixed races and individuals of our day it could not be otherwise, but we cannot deny the existence of *parallel trends* making for harmony.

Classification should thus consider blood patterns in conjunction with their physical (bodily) backgrounds rather than isolated blood groups. Notwithstanding his critical attitude toward my efforts, this is, moreover, the result of Boyd's own classification, when he divides humanity into five (or six, should we count a hypothetical, prehistoric European type) principal races as to their blood, corresponding to the White, the Mongolian, the Red, the Black, and the Australian. This classification (which bears out my argument so well) that we should think in terms of parallel patterns is practically the same as the one I proposed in 1945, except that I adduced evidence for the existence of subraces with distinctive blood characteristics and physical traits among the Whites and the Mongolians, and that I postulated the existence of an Oceanic, or Pacific, blood pattern (pp. 168–9 of the book cited). At that time I had to rely mainly on the ABO and secondarily on the MN data, and in expressing regret that I should have restricted myself to these systems Boyd does not give due consideration to the chronology of events.

Another objection was that, "Where populations, probably not closely related, proved to have about the same frequencies for A and B, [I] postulated that the A or B in one of the populations was of different intensity, which was not too clear." I had, however, quite explicitly written (p. 78 *et passim*) that blood group A covered two different A's (B existing also, though rarely, as B_2) derived from two different genes, so that between races of different color, we should be wary of our comparisons if they failed to take this fact into account. In his paper Boyd mentions, for instance, a black series from the Belgian Congo and a Chinese series from South China with very nearly the same A frequency. This similarity is, however, misleading, as the A of the Congo blacks is presumably in a proportion of at least 40% A_2, whereas the Chinese have only A_1 blood.

After having, as I trust, established my case, I will endeavor to state briefly what I have tried to contribute toward classifying human ethnic groups and races, and toward dispelling the skepticism that is perhaps more prevalent in Europe than in America regarding this new serological method of ethnic determination.

This skeptical attitude may be traced to two essential causes. Anthropologists and historians have

[1] N. Lahovary. *Les Peuples Européens*, 1st Part. La Baconnière-Neuchâtel. The book was published at the beginning of 1946, but was written mainly in 1944. See the first part dealing with serological classification and particularly pp. 90–100.

objected that practically all serological series have concerned physically undiscriminated human material. In this way the most varied physical types could be gathered in the same series, making any attempt at valid classification a forlorn venture. Second, even the results obtained under these adverse circumstances have been expressed in such a way as to leave the reader still more perplexed and confused.

Both these objections, unfortunately, contain a great deal of truth, and the second drawback has been perhaps even more responsible than the first for the rather cool reception given by many historians, physical anthropologists, and prehistorians to the ethnical applications of serology, notwithstanding the light they can shed on many of their problems.

If we consider, for instance, one of the more widely used methods in this field, the Biological Index of L. Hirszfeld, or $BI = \frac{A + AB}{B + AB}$, we note that group O, despite its importance, has been left out, so that ethnical groups far different with regard to blood and physical aspect too often share the *same* index. If, for example, we take an Armenian group with the frequencies AB 6%, A 54%, B 14%, O 26%, and another entirely different ethnical community of "Mediterraneans" (Ibero-Insular) with quite another blood pattern, such as AB 3%, A 36%, B 10%, O 51%, in both cases the resulting index would be 3! On such a basis all conclusions would be shaky, if not downright incorrect.

To avoid such errors, Melkich suggested another index, namely, $\frac{O + A}{B + AB}$. This is equally unsatisfactory, however, for it is only too obvious that the index will be the same, whether O be large and A small, or vice versa. Conclusions would, therefore, risk being just as untrustworthy as with Hirszfeld's biological index. Aware of these imperfections, L. de Hoyos proposed another index, $I = \frac{O \times 100}{A + B + AB}$. Unfortunately, the remedy cannot better the situation, for, by adding A and B together notwithstanding their antipodal character, the result would be that a Chinese group with a high frequency of B blood and a relatively low one of A would have the same index as a European group with the inverse pattern of frequencies.

O. Streng, and others with him, in the hope of avoiding these pitfalls, have had recourse to a much more complicated graphic and numerical method, founded on the ternary genotypic theory of Bernstein, according to the equation $X = \frac{2p + q}{\sqrt{3}}$. The greater complexity of the calculation and the time involved have not, unfortunately, been in any way compensated by more exact results, which are, alas, even more dismaying than those obtained by the preceding methods. Thus, Norwegians and Ethiopians are bracketed together (*I*, 38.5 and *I*, 38.4), whereas the Dutch—to mention only a very few of these startling conclusions—are sandwiched (*I*, 33.5) between the Chinese (32.9) and the gypsies (34.9), and would appear to be closely related to these two very alien groups![2]

In England, R. A. Fisher suggested the following formula: $I = \frac{A \times 100}{A + O}$, which gives fairly plausible results for the peoples of Europe, although it minimizes their differences excessively—to the extent that the southern English, the Bavarians, and the Italians of Tuscany have practically the same index; but the formula fails completely for the colored races. Using Fisher's index, the Australian aborigines are identified with the Scotch (*I*, 40.0 and 39.9, respectively), the northern Chinese with the French of Languedoc (44.1 and 45), the Chinese examined in New York would be on a par with the Danes and the South Germans, etc.

Wichniewski proposed yet another index: $\frac{O + 2A + AB}{O + 2B + AB}$. But, as Melkich showed, the index thus obtained is not satisfactory, as it arbitrarily doubles the importance of the A and B groups and accordingly minimizes that of O; whereas in reality, because of the recessive character of O, phenotypic A or B stands often for AO and BO; hence, instead of diminishing the importance of this factor, as is here the case, it would be preferable to enhance it.

Other graphic or numerical methods of representation, such as those of S. Wellisch and Avias, are equally unsatisfactory. We shall not continue to brood any longer on this comedy of errors, however, but will admit with Dürr[3] "that it is high time to give up this vain quest of an exact index of absolute values" and that a correct classification of human races and blood patterns will be much more effectively achieved by means of a comparative method that will enable us to define the *relative* position of each in respect to the other. After experimenting with various systems, the author has finally reached the conclusion that the most satisfactory, as well as the simplest and most economical of time, consists in comparing the frequencies, in one or more blood systems, of one ethnical group or race with those of other groups or races, and of summing up the differences found in the frequencies of each blood group. For the resulting total we have proposed the name "Index of Deviation." It reveals the relative biological distance separating one ethnic group from another and makes it possible to express numerically and graphically the respective position of each in a general classification.

The underlying idea is more or less similar to that of the Coefficient of Likeness of the British school of biometricians in their anthropological investigations. But their Coefficient of Likeness had a weakness in that various physical characteristics representing

[2] See O. Streng. *Die Bluteigenschaften der Völker. Festschrift f. H. Hirt.* Bd. 1 (Heidelberg, 1936), and his numerous publications in *Z. Rassenphysiol.*, between 1929 and 1941, and elsewhere.

[3] K. Dürr. *Blutgruppenauswertung für Vaterschaftsprozess, Kriminalistik und Rassenforschung.* Bern, 56–57 (1947).

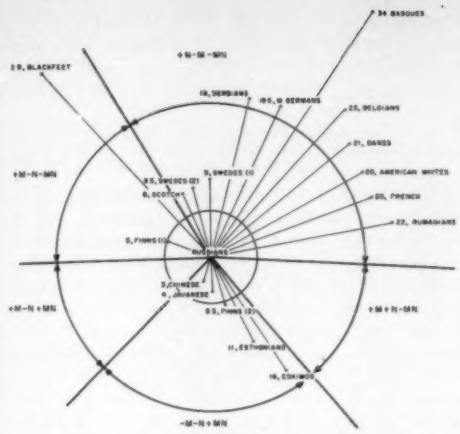

FIG. 1. Index of Deviation in the MN system between the Russians of Central Russia and other ethnic groups. The same degrees of relationship can be observed as in the ABO system. The Mongolian affinities are very striking, whereas the distance is considerable, biologically speaking, between these Russians and their German or Roumanian neighbors.

genetical and symptomological elements of perhaps very different significance were equally rated as units. In the case of the blood groups, however, this objection loses much of its weight because of their independent and simpler genetic transmission.

Were we to complement our numerical Index of Deviation with a graphic representation of the direction of the deviation observed in each case, the reader would see, at one and the same time, not only the degree of the relationship existing between the various ethnical groups under consideration (for a given blood system), but also the *direction* of the deviation. Were we to have a few *standard average series* representing the principal human blood types, it would then be easy to trace the influences causing the respective deviations and their relative strengths. In this way it would be possible to determine roughly the contribution of the various original elements to the constitution of a mixed ethnical group. Notwithstanding the very regrettable fact that there has been no discrimination of the physical types involved in connection with blood tests, and that nearly all our serological series contain heterogeneous racial elements in varying proportions, making the task of classification and correlation between blood pattern and racial type more difficult, the obstacle is not insurmountable.

Although it would greatly advance research in this field if all blood testing were done with the assistance of physical anthropologists who would define the principal physical characters of the subject tested, even under present circumstances it is possible to distinguish different blood patterns that correspond roughly to physical or racial subdivisions. Although the series tested in northwestern Europe are far from being purely "Nordic;" and those of the islanders of the Mediterranean, of the northern Welsh, and of the Berbers comprise a mixture of various physical types; whereas those of the mountaineers of the Vosges, of the Schwarzwald, of certain parts of the Alps and the Carpathians include other types besides dark-haired, broadheaded, and brachymorphic "Alpines"—nonetheless, the series of northwestern Europe are *mainly* made up of men of more or less mixed "Nordic" type, and the same relative predominance, respectively, of "Mediterranean," Iberic-Insular, and "Alpine" physical types is found in the other series.

Notwithstanding the fact that these ethnical conglomerates are not made up of "pure" races, our method of the composite average series reveals the relative predominance of a certain racial trend, which is clearly reflected in the respective blood pattern of each.

For example, an average series based on twenty of the most numerous and representative serological series of southern England, northern France, western Belgium, Holland, Denmark, western Germany, northern Switzerland, the Piedmont, and western Austria would show the following frequencies in the ABO system: AB, 3.4%; A, 43.3%; B, 9.4%; O, 43.8%. Since all the series of these various ethnical groups are closely related, as evidenced by an Index of Deviation usually less than 3 or 4 units, even if other series had been selected to make up the average

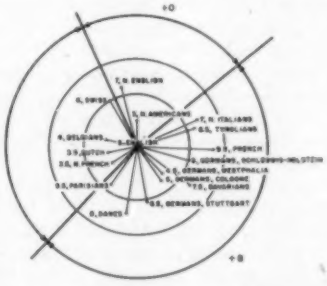

FIG. 2. Graphic representation of the serobiological relationships in the ABO system of the southern English (mean series) with other ethnical groups. The small deviations imply, more particularly so for the groups within the first circle, a very close kinship. The geographical extension is coherent and covers both sides of the lower Rhine plain and both shores of the channel with a varying inland projection. The absence of the Scotch, Irish, and northern Welsh is as significant as that, for opposite reasons, of the Scandinavians and eastern Germans.

The kinship with the northern Italians (or northern and central Spaniards and Portuguese, omitted here) is believed to be more apparent than real (notwithstanding the presence of a proportion of northern racial elements in Northern Italy and Northern Spain), inasmuch as the prevalent physical type represents a combination, in various degrees, of Alpine or Med-Armenoid and Mediterranean Ibero-Insular elements. But, as shown in this paper, a blend of the first (with a high frequency of A and a much lower one of O) with the second, having an inverse blood group ratio, would result in blood series with intermediate values, and thus pseudo-Nordic in appearance. In the case of the Italians and of the Spaniards, moreover, although our data are still scanty, this presumption is strengthened by the consideration that the frequencies of MN and A_2 are appreciably different from those of the southern English, whereas the latter are very similar to those found in the other northern groups enclosed in the above circles.

series, the difference would have been unimportant. We can thus consider our composite series as the standard one for the mainly "Nordic" population of northwestern Europe. At the same time, we should note that it reflects *racial* and not geographical conditions, for whereas the Index of Deviation is very small between, say, the southern British and the Dutch or the Germans of the lower Rhine Valley, it rises to as much as 17, or a sixfold value, in relation to the northern Welsh or northern Scotch. Likewise, the difference is great between the "Nordic" western Germans and the "Alpine" Germans of the more mountainous and secluded parts of western Germany.

When we use the same procedure for the Berbers of North Africa, certain Syrians, Greek Islanders, Sardinians, northern Welsh, northern Scotch (the last two being survivals of farflung outposts of the Mediterranean race, in the Neolithic and Bronze Ages), our synthetic average series is entirely different and is approximately as follows: AB, 2.7%; A, 32.6%; B, 9.9%; O, 54.7%. (The relationships between all the latter "Mediterranean" ethnical groups are again very close, so that another choice of individual series would, as in the preceding instance, modify the resulting average very little.)

Proceeding in the same way for the "Alpine" groups of western and central Europe, to which we can add the broadheaded Armenians, who have practically the same blood pattern, we obtain the following average standard series: AB, 3.5%; A, 55.1%; B, 8.3%; O, 33.1%. *Notwithstanding geographic propinquity and the admixture of other elements, the three principal physical white subraces have each a most distinctive and specific blood pattern.* The recognition of these three standard series makes it easy to understand why, for instance, in Italy (Tuscany, former Kingdom of Naples), on the English-Welsh border, and in northern England, the frequency of A decreases and that of B or O tends to increase. This is evidently due to "Mediterranean" influences, for the "Mediterranean" blood patterns have these characteristics in a still more accentuated form. If, on the other hand, the Scandinavians have a greater proportion of A and a lower frequency of O than the British or the western Germans, this is undoubtedly due to "Alpine" or Lapp influences, and the situation is all the easier to explain if we remember that southwestern Norway is inhabited by an important minority of rather dark broadheads and that the Lapps of northern Scandinavia (and probably the more ancient populations that preceded them) have an ABO blood pattern very similar to that of the "Alpines." The usefulness of these "standard series," notwithstanding their approximative character, is thus obvious for human classification, as can be shown also from other examples. It had long been asserted that the broadheaded populations of Russia and of some of her Slav neighbors were related to the "Alpines" of western Europe and the Carpathians. With the application of our standard series, this myth can at once be exploded, as a comparison of the standard "Alpine" and an average Russian series, composed along the same lines, reveals the differences at a glance:

Alpine series.....AB, 3.5%; A, 55.1%; B, 8.3%; O, 33.1%
Russian composite series
AB, 8.2%; A, 34.9%; B, 24.4%; O, 32.5%
Eurasiatic and northern Asiatic composite series
AB, 8.2%; A, 32.1%; B, 28.7%; O, 31%

It is therefore evident that, whereas the Alpine and Russian or East Slavonic broadheads are not connected, the latter have very near relations in the broadheads of the Mongolian races of northern Asia, the Index of Deviation being no less than 43 between "Alpines" and "Russians" and only 8.5 between the Russian and Asiatic series. Furthermore, not all these Russians are broadheaded, so that the difference would have been even greater if the less brachycephalic northern European elements had been sifted out of the Russian series, in which the broadheads are the more specifically Asiatic. The European broadheads are thus quite as "European" as the "Nordics" and have no relation with the broadheads of Mongolian, or Finno-Ugrian and Turkish origin, for the Index of Deviation is as high as 50. The origin of the "Alpines" should thus be no longer sought in Asia, because their ABO and MN blood patterns are both entirely different from those of the Mongoloid races. This is probably true also of their Rh frequencies, though we still lack conclusive data as to that.

Our standard series will enable us to clear up yet another problem that has been the cause of perplexity and has led to speculative conclusions: the resemblance of the ABO pattern of several sections of the Spanish population with that of the Scandinavians, though this resemblance is not supported by the predominant physical types of the respective ethnic groups (nor by their MN blood pattern or Rh frequencies). If we turn our attention to the fact *that the combination* of an "Alpine" *with* a "Mediterranean" series would give as an end result, something very similar to these perplexing Spanish series in the ABO system, the key to the mystery seems to have

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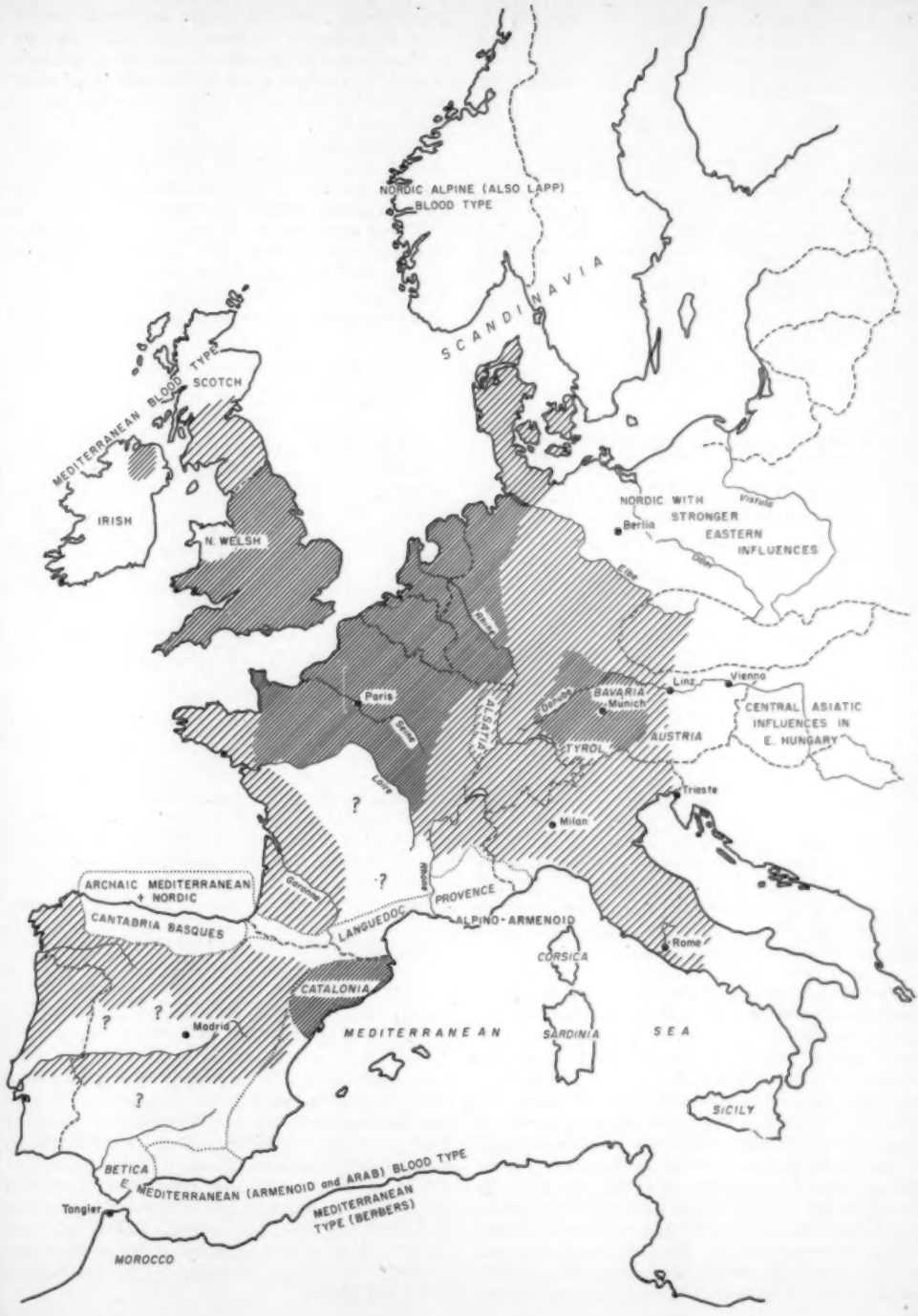
FIG. 3. Bioserological relationships of the West and of the English. Mean series of 227,251 English of the south of England: AB, 3.1%; A, 43.6%; B, 8.4%; O, 44.9%. Unshaded areas show geographical location of continental Europeans most closely related bioserologically to the English (less than 6 D.C. units in the ABO or MN systems). Bands show related populations, but mixed with other elements, prevalently "Alpine" or "Mediterranean," according to the region, which somewhat dilute the kinship with the dominant component of the English. The connection with northern Italy, central Spain, and Portugal might be more apparent than real and be the result of convergence, as shown elsewhere. In Catalonia, however, the "Nordic" element is probably more strongly represented, and the kinship in this case is doubtless more consonant with reality than in the rest of Spain, or in Italy, the physical aspect of the population being here less divergent from that of northwestern Europe. It will be noted that the Celtic-speaking members of the British community, as well as the Scotch, and even the Bretons of France, are but little or not at all related to the English, who thus appear to be essentially of western Germanic origin, although the original Celts were much nearer the Germanic type than the "Celts" of today.


NORDIC ALPINE (ALSO LAPP) BLOOD TYPE
SCANDINAVIA
MEDITERRANEAN BLOOD TYPE
SCOTCH
IRISH
N. WELSH
NORDIC WITH STRONGER EASTERN INFLUENCES
Berlin
Vistula
Oder
Elbe
Rhine
Paris
Seine
Loire
ALSATIA
Danube
BAVARIA
Munich
Linz
Vienna
AUSTRIA
CENTRAL ASIATIC INFLUENCES IN E. HUNGARY
TYROL
Trieste
Milan
ARCHAIC MEDITERRANEAN + NORDIC
Garonne
CANTABRIA BASQUES
Rhone
PROVENCE
LANGUEDOC
ALPINO-ARMENOID
CORSICA
Rome
CATALONIA
Madrid
MEDITERRANEAN
SARDINIA
SEA
SICILY
BETICA
E. MEDITERRANEAN (ARMENOID and ARAB) BLOOD TYPE
Tangier
MEDITERRANEAN TYPE (BERBERS)
MOROCCO

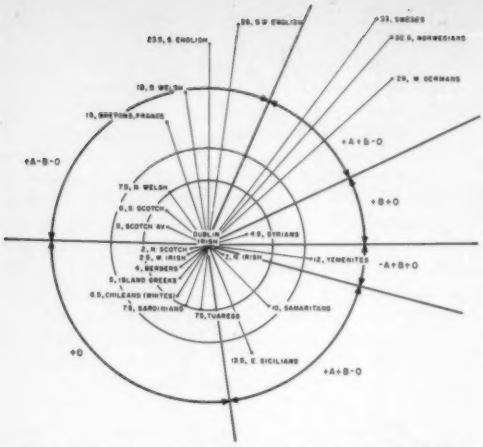


FIG. 4. Irish blood affinities in the ABO system. Scale, 5 mm = 1 deviation unit. Dublin series, 2435 cases; AB, 2.6%; A, 32.3%; B, 11.4%; O, 53.6% (Sachs). The ethnic groups inside the inner circle (6 deviation units from the Dublin Irish) would appear to be the most closely related to these Irish. They all belong to the "Mediterranean" physical race. The high frequency of A_2 and of rr in the Irish are two other peculiarities they share with "Mediterraneans," such as the Basques and other Iberians and Sardinians (as to A_2). We know that these, at first sight, rather startling affinities are easily explained on historical grounds, since the inhabitants of Ireland and the major part of the British Isles during Neolithic times and a great part of the Bronze Age belonged nearly exclusively to the Ibero-Insular fraction of the Mediterranean race, having come probably from Spain, and originally, it would seem, from North Africa. The Celtic and later massive Anglo-Saxon migrations destroyed or dispersed the descendants of these early races in the fertile parts of England and Scotland, while these succeeded in surviving in the poorer mountainous west and in Ireland, after adopting the language of their Celtic conquerors, who do not seem to have been as numerous in these regions as was once believed. Modern linguists have demonstrated conclusively that the syntax and the idioms of Welsh and Gaelic present to this day remarkable similarities with Pharaonic Egyptian of the early and middle Empire. These ancient influences doubtless explain the somewhat unexpected kinships of the Irish. It is also possible, however, that insularity and endogamy, as in other instances, may have contributed to lower the A frequency and to increase the proportion of O blood, giving in this way the impression that the Irish blood pattern was more like the Mediterranean pattern than it would have been otherwise. At any rate, the part played by the Scandinavians in the peopling of Ireland (with the exception, perhaps, of Ulster) seems to have been considerably overrated.

been found. The verisimilitude of this solution is supported by the existence of typical Armenoid series, with Arab admixture, in many parts of southern Spain, as well as by the presence of more purely European Alpines in the Pyrenean provinces and in some other regions of northern Spain. It should be noted, also, that the Basque blood pattern, which corresponds presumably to that of a much larger part of ancient Spain than its restricted modern homeland, presents a somewhat higher frequency of A blood than the North African or insular Mediterranean series. This fact may help to explain the rather high A frequency in many Spanish groups without invoking exclusively the admixture of a great proportion of "Alpino-Armenoids." It can be added that the existence of Armenoid eastern Mediterranean blood in a large part of southern Spain finds support in archaeology and prehistory, for civilization was brought to southern Spain in the early metal ages by extensive immigration from the eastern shores of the Mediterranean.

We have chosen phenotypic series for purposes of classification because in the genotypic system the AB group is unduly minimized notwithstanding its racial significance. Myslaveč had already shown in 1944 and 1945 that the Bernstein theory passes too lightly over observed facts, the frequency of the AB group conforming to expectation in the whites and, to a more limited extent, in the blacks, whereas it is much higher than the expected values in the Mongoloids and in the

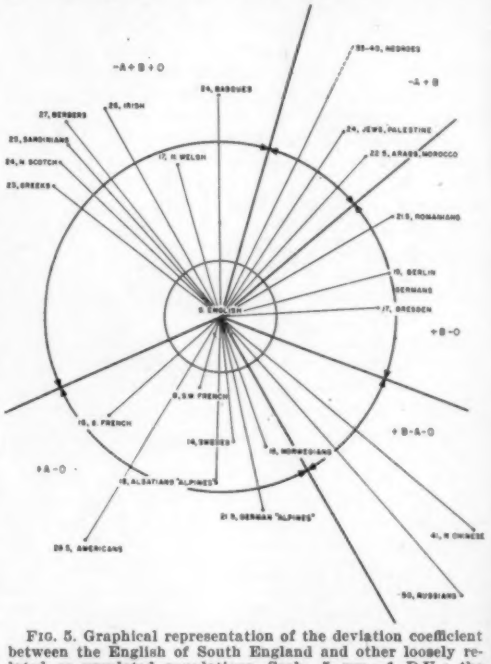


FIG. 5. Graphical representation of the deviation coefficient between the English of South England and other loosely related or unrelated populations. Scale, 5 mm = 1 D.U.; the direction of the deviations, marking out ethnical families, is shown in the margins. It will be observed that the Russians from Moscow stand even farther from the South English than do the North Chinese or Negroes. The figures are in round numbers.

populations with a Mongoloid or Eurasiatic admixture. This excess evidently has a racial significance. Myslaveč assumes that this racial trait is probably due to a slightly different position of the respective genes in the yellow races, favoring certain linkages.

Thus, in the white fringe, a higher frequency of AB than the expected value is a diagnostic indication, of Asiatic admixture, just as the existence of sickle-shaped cells is usually evidence of Negro admixture in North Africa and other zones of contact between whites and blacks.

Another observation should be made concerning the O group. I have shown elsewhere[4] that, as a rule, its frequency grows in proportion with the isolation and numerical weakness of the community concerned. O blood are offshoots of lowland populations where the frequency of this group was on an average slightly less than 45%. It cannot be said, either, that these mountaineers may represent very ancient residues of

TABLE 1

FREQUENCIES IN THE ABO SYSTEM

		AB (%)	A (%)	B (%)	O (%)	Synthetic series
I.	Whites					
	a) Mainly "Nordic" type	3.4	43.3	9.4	43.8	Of the A total *ca.* 25% A_2
	b) " "Mediterranean" type	2.5	32.0	10.0	55.5	" " " " slightly more A_2
	c) " Alpino-Armenoid	4.8	54.7	9.7	31.7	" " " " ——— ——
	d) " Semito-Arabic	6.5	34.8	19.0	39.5	" " " " ——— ——
	e) Archaic Mediterranean, Basques, Moulinier	1.0	38.4	2.7	57.9	" " " " slightly more A_2
II.	Eurasiatics and Mongoloids					
	f) Av mean, Russians of Russian Europe	8.2	34.9	24.4	32.5	No data at hand
	g) Av mean, North Asiatics (Manchurians, Chinese, Wotyaks, Siberian tribes, Turkmenes, Mongolians)	8.2	32.9	28.3	30.8	No A_2
	h) South Asiatics and Indonesians	5.3	23.1	28.6	43.3	" "
	i) North American Indians (Blackfeet and other mixed tribes not included)	0.0	9.0	1.0	90.0	" "
	Av South American Indians, when pure blood	0.0	0.0	0.0	100.0	" "
III.						
	j) Negroes, av series	4.4	24.3	24.8	48.5	Av *ca.* 40% A_2, or more
	k) Pygmies, conflicting series, but frequency of A seems to be greater and that of O significantly smaller than in the Negroes	—	—	—	—	?
IV.						
	l) Australian natives, mean various authors	0.6	48.1	2.4	48.9	No A_2
V.	Pacific Islanders					
	m) Polynesians, Maoris, etc.	0.5	59.0	2.0	38.5	" "

Richter noted this fact in Germany, but recent work in the mountains of Switzerland has brought out new and cogent reasons for believing that, in the course of time, small endogamous communities tend toward an ever-increasing frequency of the O group.[5] It is as yet difficult to say whether the bearers of the O blood have higher resistance to some forms of sickness, or for what reason the O's multiply under these conditions, but there is no gainsaying the fact that the proportion of the O's increases, especially in Europe, with elevation and with the degree of isolation. In Switzerland, in the plains and at the mouths of the valleys, the frequency of O is around 45%, but it rises with elevation, reaching 50%, then 55%, and finally 60% in the highest and most secluded villages at the upper ends of the valleys. The phenomenon has been observed on the northern slopes of the Alps, among the German Swiss of the upper Rhine Valley, as well as on the southern slopes of the Alps, among the Italian Swiss in the higher parts of the Calanda Valley. Ethnic affiliations do not affect the factor at play, for these villagers with a frequency of some 60% former populations with a higher frequency of O, for in the case at least of the German-Swiss villagers just mentioned, the dates of their settlements are known, and the valleys were not inhabited before their arrival. It is not surprising, therefore, that O blood should be particularly frequent among the Bedouin of the Syrian Desert, the inhabitants of other deserts, and islanders. It seems doubtful, consequently, that, when these conditions of isolation are present, the O group should have the same value for the classification of human communities as the other groups. In fact, it appears as if it were a better index to the length of time these small clusters have been isolated and endogamous. The high frequency of O blood among the natives of America signifies the prolonged existence of small, isolated clusters of roving hunters rather than an inherent racial trait. This would explain the large discrepancy between the American-Indian blood pattern and that of the northern Asiatics in the ABO system, whereas the other systems evince an undoubted relationship. If some American Indian tribes, such as the Blackfeet, have a significant proportion of A or B blood the cause might be sought in a comparatively recent admixture of European, or eventually Negro, blood; in a relatively late date of arrival in America, in which case the blood pattern would have retained more traces of Asiatic origin;

[4] N. Lahovary. Nouvelles considèrations sur la valeur du groupe O pour les determinations ethniques. O groupe d'aboutissement? *Bull. soc. suisse d'anthrop.* (1951).

[5] W. Knoll. Blutgruppen Bestimmungen bei den Walsern in Rheinwald und oberen Avers. *Bull. soc. suisse d'anthrop.* (1950).

TABLE 2

FREQUENCIES OF M AND N*

			M%	N%
I.	Northwestern European, prevailingly "Nordic," mean		29.0	21.5
	"Alpine" and Armenoid (Ramneamtzu, Boyd, *et al.*)		32.0	21.0
	Western Mediterranean (Spain) data too scanty to be conclusive. (Agosti; small Basque series (Mourant) as high as 27.4% N)		22.4	25.2
	Eastern and Central Mediterranean (Syrians, Boyd; North Centr. Italians, Ponzi; perhaps Welsh, Boyd) mean		29.0	16.5
	Egyptians (Boyd)		27.0	20.0
	The Scandinavians, Icelanders, Scotch, Ests, and Western Finns seem to represent a transition between the "Nordic" frequencies and the Russian and Eurasiatic type, as can be seen from the following series:			
	Swedes (Wolff, Jonsson, 1200)		36.5	17.5
	Scotch, Glasgow (Matta)		35.0	17.1
	Icelanders (Mourant, 747)		31.2	17.3
	" students (Mourant, only 205)		41.0	16.1
	Finns, Western Finland, probably of partly Swedish descent (Mustakallis)		37.1	15.7
	Esthonians branch of the Finns (Rooks)		34.8	15.4
II.	Northern Eurasiatic and Mongolian type			
Eurasiatic and Mongolian	European Russians, Moscow region (Boyd)	Large excess of M with increasing values	40.0	16.0
	Chinese, Canton (Boyd and Alley)		38.6	15.8
	Javanese (Postmus and others)		38.2	14.9
	Finns, of Finland (Streng, about 6900 cases)		42.3	13.7
	Latvians (Race, Sanger, Keetch)		45.3	11.0
	Eskimos, Western Alaska (Matson, Roberts)		47.8	10.5
	Finns, of Eastern Finland (Streng)		47.1	11.4
	(The last are intermediate between the north Asiatic and the American-Indian type of frequency, with little, or practically no N)			
Extreme Mongolian	Utes (Matson and Piper)		58.6	6.7
	Mapuchos, Chile (Sandoval)		57.0	9.0
	Pueblo Indians (Hillen, Larsen)		59.3	7.8
	American Indians (Boyd)		58.3	5.0
	" " (Levine and Landsteiner)		60.0	4.9
	Eskimos, Alaska (Levine)		—	4.7
	Greenlanders (Hanssen, 570 cases)		83.5	0.9
	South American Indians, Matto Grosso, Brazil (Pasqualin, Ottensooser)		80.0	0.7
III. African Blacks	Negroes, mean (Wiener, Belkin, Dujarric, *et al.*)		28.5	27.5
	Pygmies, Belgian Congo (Jadin)		29.3	26.1
IV. and V. Oceanic type	Ainus, Fadoo Uibo	Large excess of N and trend toward the absence of M	17.8	31.9
	New Caledonians (Melanesians) (Avias)		9.1	49.8
	Australian natives (Cleland)		3.0	67.4
	" " Western Australia (Boyd)		3.3	71.2

* Typical of the various human races (in round numbers). (Due to lack, as yet, of sufficient data for comparative purposes of the more recently discovered S quality, we will not take it into consideration.)

or in a combination of both causes. (It should not be forgotten that A blood frequencies are fairly high in northeastern Asia and among some Eskimo tribes.)

The yellow race presents a blood pattern which differs more pronouncedly from that of the white races than that of the latter differs from the pattern of the black races of Africa in certain respects, such as the absence of A_2 and of Rh negative, the much higher proportion of M, the tendency of N toward zero, and, more particularly in inner Asia, the very high proportion of B. The Australians and the American Indians, who are at opposite poles with respect to the frequencies of A and O, of M and N, and probably also of most other blood groups, are at the same time those who differ the most from the whites.

In respect to the Rh system, the quarrel over terminologies between the American and the British schools has made exact comparisons between series difficult, but we know there are general trends that are specific within each of the big racial entities. Thus, in the black race we find the highest frequency of R_0 (cDe) blood (42% and over), whereas the proportion falls to 11% in Egypt, lower in Iraq, and approaches zero in northern Europe. The Rh_1 (CDe) group, which is, in contrast, less frequent among the blacks (21% in the blacks of America, but probably less in Africa, where the Pygmies have only 6% Rh_1 [i.e., $R_1R_$] blood, in the limited series tested so far), is prevalent in Europe, particularly in southern Europe (Sardinia, 77%) and reaches its maximum in southeastern Asia and Oceania, with 90–93%. The Rh_2 (cDE) frequencies show similar racial correlations. This factor is comparatively rare among the "Mediterraneans" (some 7–9%), but it increases to 13% in northwestern Europe, to about 16% in eastern Europe, reaching nearly 30% among some North American tribes. In the Indonesian and Oceanic blood patterns it tends to be absent (*ca.* 2%).

The P+ factor contributes its effect on the specificity of the various racial groups, its frequency nearly touching the 100% mark in the Negroes of Africa, whereas it oscillates between 60 and 70% among the Japanese and Indonesians, with intermediate values of 75–80% in the whites. The newly discovered Duffy (Fy) group also has a specific racial repartition. In the series recently tested, the Negroes have presented the lowest percentage (26%), the opposite extreme being found in the Chinese and American Indians with nearly 100%, whereas the whites again stand in between, with 65% in the British. More extensive tests might modify these results to some extent, but it is probable that, generally speaking, they already give a true picture.

However, our data are still scanty, apart from the ABO, MN, and Rh systems, which must thus serve as the bases for the only classification actually possible, taking into account that the Rh data are much less complete than could be wished.

The average representative series presented here are necessarily approximations, for the basic material is more or less heterogeneous; but, even so, the author believes they give a sufficiently clear picture of the specificity of the various races and subraces and allow a reliable classification, with the Index of Deviation helping us to define numerically the relative kinships—or to stress the absence of any biological relationship when the rating is too high. Beginning with the ABO system, our classification forms the picture shown in Table 1.

Although less material is at hand for the MN system (and so little for the S factor that we are obliged to leave it out of consideration), the frequencies in this system support the general pattern sketched above (Table 2).

TABLE 3

PRINCIPAL FREQUENCIES IN THE RH SYSTEM
(PERCENTAGES)

	Rh_1 and R_1R (CDe/CDe)	Rh_1R_2 (CDe/cDE)	Rh_2R (cDE/cde)	Rh_0 (cDe/cde)	rr (Rh negative)
I. *Western European pattern*					
English, mean (various authors)	54.9	12	12.2	2.4	13
French (see Barnicott)	55.6	12.2	12.7	2.5	14
Whites, New York (Levine and Landsteiner)	54.4	15	13.7	2.4	13
North European, with a slight trend toward Eurasiatic frequencies					
Norwegians (Mourant *et al.*)	52.3	*ca.* 18.5	13.7	0.4	13.7
Icelanders (Mourant *et al.*)	51.2	17.1	15.6	1.5	14.1
Latvians (Mourant *et al.*)	50.3	18.2	15.7	0.6	13.4
"Mediterraneans" of various subtypes					
Spaniards of Catalonia	63.2	9.4	12.8	0.6	13.1
Spaniards, Galicia (Mourant *et al.*)	66.9	12.4	9.3	3.1	5.1
Egyptians (Mourant, Ibrahim, *et al.*)	65.2	8.1	9.0	10.9	5.9
Sardinians (Sassari, Morganti)	76.0	—	—	—	4.0
Southern Italians, Naples (Sassari, Morganti)	66.0	—	—	—	8.0
South European type with high *rr* frequency					
Basques (Moulinier, Mourant, *et al.*)	55.8	6.8	7.6	0.5	*ca.* 30
French, Southwest (Ringenbacher)	—	—	—	—	20
Italians, N. Italy (Morganti *et al.*) (The Irish seem to belong to the same type)	57.0	—	—	—	*ca.* 18
II. *Northern Asiatic and American pattern*					
Japanese in America (Weiner *et al.*)	37.5	47.2	13.3	0.0	0.1
Chinese	—	—	—	—	0.5
Utes, Utah (Matson *et al.*)	37.5	32 (?)	28.9	0.0	0.0
Eskimos, Western Alaska (Roberts *et al.*)	34.9	42 (?)	19.6	0.0	0.0
Mexican Indians (Comas)	48.0	42	9.2	1.0	0.0
III.					
Negroes, in America (Wiener *et al.*)	21.2	7	22	42	6.0
Pygmies, Belgian Congo, small and not conclusive series	6	—	19.5	63.8	10.5
IV and V. *Indonesian-Pacific pattern*					
Javanese	75.0	22.0	2.0	0.0	0.0
New Caledonians (Avias)	78.9	17 (?)	2.3	0.0	0.0
Papuans	93.0	4.0	3.0	0.0	0.0
Aborigines of the Philippines	90.0	?	?	0.0	0.0

TABLE 4

INDEX OF DEVIATION (IN ROUND NUMBERS) IN THE ABO, MN, AND RH SYSTEMS

	ABO	MN	Rh (5 principal reactions)	Total index of deviation (phenotypes)
Between "Nordic" whites and Russians in Europe (av series)	39	17.5	Inadequate data at hand	
Between Nordic whites and North Asiatic (Japanese for Rh)	38	17	68 (65‡)	120
Between Nordic whites and Negroes (av series)	38	6.5	96	142
Between Nordic whites and Mexican Indians and Pueblos	*ca.* 100	*ca.* 45*	*ca.* 51	*ca.* 196
Between Nordic whites and North Caledonians (Melanesians)	20†	48	55	133 (123!)
Between Nordic whites and Western Mediterraneans	22	10 (Spain)	30	62
Between Western Mediterranean type (Berber, Northern Welsh, Sardinian, Greek Islanders, and Negroes) (av series)	33	8	97	138
Between Western Mediterranean and American Indians (Mexican and Pueblos)	*ca.* 70	55	45	170
Between Western Mediterranean and Northern Asiatics	45	26	84	155
Between Western Mediterranean and North Caledonians (Melanesians)	6‡	38	45	89
Between Northern Asiatics and Negroes (Japanese for Rh)	27.5‡	23	113	163.5
Between Northern Asiatics and North Caledonians (Melanesians)	43	65	82	190
Between Northern Asiatics and American Indians (Mexican Indians for Rh)	110	30	20	160
Between Negroes and American Indians (Mexican Indians for Rh)	86	51	132	269
Between Negroes and North Caledonians	31	41	136	208
Between Southern Asiatics (×Indonesians) and New Caledonians	39	64	9	112

* The Pueblos are taken as representative of the average North American Indians.

† If the absence of A_2 in the blood of the North Caledonians is taken into account, the difference between the Western Mediterranean ABO pattern and that of the North Caledonian, or between the latter and that of the other whites, is greater than these numbers would show.

‡ Same observation for the respective cases.

The Japanese (Furuhata, 17,000 cases) manifest their mixed Mongolian and Oceanic ancestry with the Mongolian strain bringing the M blood and the Oceanic-Ainu atavism raising the percentage of N considerably above that of the purer Mongolians, while lowering that of M notably below that of the Chinese or Eurasians. The similitude of the Japanese type with the European frequencies would thus be the result of convergence. Apart from the Japanese and the Ainus, who have Oceanic and Indonesian affinities, the Mongoloid nations of Asia can be divided into two great subraces, the Northern Asiatic and the Southeastern Asiatic; the American Indians in the MN system show a specialized, extreme form of a North Asiatic trend, which is also pronounced in the Eskimos. As in the ABO system, the Pacific islanders have also a highly specialized position in the MN system. In both cases it is interesting to note that this specialization has had an exactly opposite trend to that of the American Indians. These two ethnic groups represent in this respect the two opposite poles in human blood patterns.

Ethnic data for the Rh system (Table 3) are still comparatively scarce, and leave large gaps in our knowledge. However, although we cannot consider them as conclusive, they are in harmony with the classification based on the two former systems. Notwithstanding the independent transmission of the various blood groups, their degrees of frequency form quite distinctive patterns, corresponding on the whole to the principal physical races and subraces, even though these are mostly mixed with heterogeneous elements. The various color lines are by no means empty abstractions, but express deep-seated and fundamental biological and organic differences.

Although the indications given by the ABO and MN systems generally parallel those of the Rh system, there are a few interesting exceptions, which as a rule are due to mixed origins, with one ancestral line contributing the pattern of a certain system, and other lines bequeathing the pattern of another system. Thus the Northern and Southern Asiatics excluding India, which has Mediterranean links, share the same type of frequencies in the MN system, but differ considerably in the ABO and Rh systems. The Southeastern Asiatics reveal an Indian and an Oceanic trend, which would be in accordance both with the Indian substrata attributed to Indonesia and with the partly Indonesian origin that archaeology assigns to the Pacific islanders.

The American Indians manifest most distinctly their North Asiatic affinities by their MN and Rh blood patterns, even if we should ignore the absence of A_2 and the very high frequency of the Fy^a factor they share with these Asiatics. The divergence related to the prevalence of O in the American natives would lose much of its racial significance if the views of the author were admitted. It seems, therefore, that we can distinguish in the American Indians, as in the Eskimos, branches of the North Mongoloid family, with specialized characteristics resulting from their long isolation and their life in small communities in sparsely peopled territories or ice wastes.

The author does not share the views expressed in these columns by Boyd that a distinctive Pacific blood pattern does not exist. Although the blood patterns of the various populations of Oceania and the Pacific are not all alike—which is quite natural if we consider the great physical differences these peoples present—there are, nonetheless, specific Oceanian traits. One example is the very high percentage of the Rh_1 and A blood groups, in marked contrast with the Asiatics and the Negroes, notwithstanding the black hue of the Australians and the Mongoloid features of some of the Polynesians. The absence of rr (cde/cde) and of A_2 would, it is true, bring these Oceanians nearer to the Mongoloids, but otherwise the frequencies in the ABO system, in particular of the Polynesians, bear a striking resemblance to the percentages found in the less hybridized and more archaic sections of the "Alpino-Armenoid" fraction of the white race, whereas the high rate of Rh_1 (R_1 R.) brings them nearer to the Mediterranean whites. All the authors who have studied the problem have agreed that the Polynesians undoubtedly have a Europoid component. As the "Armenoids" of western Asia are tall, dark-haired, and brachycephalic like the Polynesians, who, in the upper classes, make much of their relatively light complexion, we could presume that before later admixtures the original Polynesians were largely Europoid, tracing their origin to the country around the Persian Gulf, where groups of broadheads (probably outcrops of the Armenoid block) are still to be found among "Mediterranean" populations of the Semitic variety.

The Index of Deviation will allow the reader to visualize even more clearly the results and the grounds of our classification. Lacking sufficient data for the frequencies of A_2, we shall omit them from consideration. However, as we know that roughly 25% of the European A blood is really A_2, whereas the Mongolians and Oceanians have only A_1, the Index of Deviation between Europeans and these races should be raised by several units, whereas the resulting difference with the blacks, who have the most A_2 blood, would be so much smaller. The numbers given for the deviations between whites and Mongoloids or Oceanics thus appear somewhat smaller than they should be.

The numbers we see listed in Table 4, although representing merely approximations or, rather, indicative values, give us nevertheless a fairly adequate picture of racial relationships. This picture is supported in a general way by archaeological or historical evidence, as well as by physical anthropological data. The differences between the "Nordic" or "Mediterranean" whites and the Mongolian races of Asia, or the Negroes of Africa, are in all cases very great. Yet it is suggestive to observe that, as expected, the difference between "Nordic" whites and northern Asiatics is somewhat less than that between the same whites and the blacks of Africa, whereas we have the *inverse ratio* between western "Mediterranean" whites and these colored races.

At the same time it is interesting to note that, as expected, the difference in blood between the north Asiatic and the Pacific peoples is much greater than that between the latter and the Indonesians; on the other hand, notwithstanding the bond of color, the African Negroes differ more in this respect from the Melanesians than from the whites, or even the Mongolians. It might be mentioned also that the Negroes are somewhat farther from the northern Asiatics than from the whites, particularly in the case of the Ibero-Insular subrace; the Negroes, moreover, share with the whites the A_2 and rr blood factors. The Pacific blacks and the African blacks thus show no connection in their blood. It even looks as if the difference were somewhat less great between the western Mediterraneans and the Oceanians (if we take into account the lack of A_2 in the Oceanians, the total Index of Deviation would reach *ca.* 100, instead of 89, as indicated). The Caucasoid traits (Armenoid in the Polynesians, and Semitic in the Melanesians) found in the Oceanians might explain this peculiarity to some extent.

Figs. 1–5 will allow the reader to visualize the author's method and the results that can be attained by using the ABO, or any other system, in classifying the various ethnical groups and races, with their reciprocal connections or, as the case may be, their divergence.

EDITORS' NOTE: *An unusable draft of this article was submitted in July 1951, and it has been slow work to put in proper form for publication. Meanwhile research has continued in this live field, and the author will be accorded the opportunity of bringing the subject up to date in a subsequent communication.*

News and Notes

Southeastern Society of Ichthyologists and Herpetologists

THE second annual meeting of the Southeastern Society of Ichthyologists and Herpetologists (formerly the Southeastern Herpetological Society) was held on Oct. 24–25, at the University of Alabama in Tuscaloosa. Thirty-five people, representing 14 institutions, attended the sessions. The varied program included research papers, institutional reports, examination of vertebrate collections of the University of Alabama, and Saturday afternoon field trips.

A report by Clarence H. Shockley, of the University of Mississippi, discussed the effect of mammalian gonadotropins, FSH and LH, on two-year-old male water snakes. In contrast to the situation in birds and mammals, where the specificity of response to each gonadotropin is distinct and separate, he found that in snakes each gonadotropic fraction was able to produce some effects of the other fraction.

Changes in nomenclature were suggested for two different groups of snakes. Wilfred T. Neill, of the Reptile Institute at Silver Springs, Fla., reviewed the taxonomy, nomenclature, and natural history of the rainbow snake, *Abastor erythrogrammus*. He found overlapping morphological differences between this species and the mud snake, but the separation between the two is largely an ecological one. He concluded that the rainbow snake should be transferred to the genus *Farancia*. After a study of the racers and whipsnakes of the genera *Coluber* and *Masticophis*, Walter Auffenberg, of the University of Florida, found only slight differences that do not merit generic separation, and he suggested that the two groups be reunited in the genus *Coluber*.

The four elements that comprise the fish fauna of the northern Gulf coast at Alligator Harbor, Fla., were described by Edwin B. Joseph, of Florida State University. Analysis of 108 species revealed that the largest group of fishes was characteristic of tropical waters, the second of temperate waters, a third was endemic to the Gulf of Mexico, and the fourth faunal component included species restricted to the Gulf and southeastern coast of the United States.

At the business session plans were made to present to the American Society of Ichthyologists and Herpetologists a formal request that this regional organization be recognized as a Southeastern Division of the national society, embracing Virginia, North Carolina, South Carolina, Georgia, Florida, Alabama, Mississippi, Louisiana, Tennessee, Kentucky, and the District of Columbia. Officers elected for 1953 were: president, Ralph W. Yerger, Florida State University; vice president, Donald C. Scott, University of Georgia; secretary-treasurer, Wilfred T. Neill, Reptile Institute, Silver Springs, Fla.

The third annual meeting is scheduled for the fall of 1953 at the University of Georgia in Athens. A symposium on the "Factors Affecting Distribution of Poikilothermic Vertebrates in the Southeastern States" is being planned for this occasion.

RALPH W. YERGER

Department of Zoology
Florida State University

Scientists in the News

Paul J. Anderson, chief of the Tobacco Laboratory of the Connecticut Agricultural Experiment Station, will retire on April 1. **William L. Slate,** director emeritus, will fill the post until a permanent successor is named.

L. M. N. Bach, associate professor of physiology at Tulane University, was appointed executive director of the Survey of Physiological Science, effective Mar. 1. He has taken a year's leave of absence in order to launch the survey's second and definitive phase. **Orr E. Reynolds,** who directed the study during its pilot phase, has returned to his duties as director of the Biological Sciences Division at the Office of Naval Research. The Survey of Physiological Science is the American Physiological Society's 27-month project to examine the status of physiology throughout the U. S. Supported by a grant from the National Science Foundation, it is guided by a committee representing universities, industry, and government (SCIENCE, 115, p. 3 [June 20, 1952]).

B. E. Bassett, vice president of Olin Industries, has been appointed general manager of the United States Defense Corporation, an Olin subsidiary, which is operating the Ammunition Division of the St. Louis Ordnance plant. Mr. Bassett has been with Olin since 1936, and was general manager of the United States Cartridge Company, which operated the government-owned St. Louis Ordnance Plant during World War II.

John Z. Bowers, dean of the University of Utah College of Medicine, has been requested by the Ford Foundation and the government of India to organize a project in public health training, to be based on recommendations made by Dr. Bowers following his mission to India last summer. He will revisit India for a period of two months, leaving Mar. 15.

Carl F. Cori, of Washington University, St. Louis, will give the 1953 Silliman Lectures, on "Enzymes and Regulators of Carbohydrate Metabolism," at Yale University, Mar. 19–27. All lectures will be given at 4:30 P.M., the first and last in Sterling Law Library, the others in Room 160, Sterling Chemistry Laboratory, and are open to the public without charge.

John S. Diekhoff, formerly director of the Center for the Study of Liberal Education for Adults in

Chicago, has been appointed professor of education at Hunter College. From 1943 to 1946 Dr. Diekhoff served as chief of the language training section in the office of the director of military training of the Army.

Evarts Graham has received the cross of l'Ordre de la Legion d'Honneur, a medal conferred as a reward for distinguished civil or military service by the government of France. Dr. Graham is Bixby professor emeritus of surgery, Washington University, St. Louis.

John D. Roberts, associate professor of organic chemistry at MIT, has been appointed professor of organic chemistry at California Institute of Technology, where he will join the staff about July 1. A Guggenheim Fellow for 1952–53, and on a year's leave of absence from MIT, Dr. Roberts has been conducting research at Caltech on the theory of the structure of organic compounds. He will leave in March on a 10-week trip to England, France, and Switzerland to continue his research.

Walter Orr Roberts, of the High Altitude Observatory of Harvard University and the University of Colorado, Boulder, will discuss "Unsolved Problems of the Sun's Atmosphere," as a Sigma XI national lecturer, at a number of colleges and universities in the South and Southeast during March.

A. H. Van Landingham has been designated acting dean of West Virginia University's College of Agriculture, Forestry, and Home Economics and acting director of the Agricultural Experiment Station. Dr. Van Landingham has been assistant dean and director since 1950, and will fill a temporary vacancy created by a year's leave of absence granted **Harry R. Varney** for service as chief of staff of the Senate Committee on Agriculture and Forestry.

Theodore von Karman will lecture on "Aerothermodynamics and Combustion Theory," on Mar. 24, 25, and 27, in Frick Auditorium, under the sponsorship of the Daniel and Florence Guggenheim Jet Propulsion Center, Princeton University.

Martin G. Weiss has been named research director of field crops in the Bureau of Plant Industry, Soils and Agricultural Engineering, USDA. He was named project leader in soybean investigations for the bureau in 1950, and will continue to direct the soybean project in addition to his new duties.

S. Husain Zaheer, director, Central Laboratories for Scientific and Industrial Research and professor and head of the Department of Chemical Technology, Osmania University, India, will visit Europe and the U. S. this month on a United Nations Economic Development Senior Fellowship. He will study various industries, especially coal, ceramics, oils, and fine chemicals, with regard to their relation with research laboratories, their developmental projects, and completed processes for large-scale manufacture.

Education

The American College of Allergists will sponsor a graduate course in allergy at the Conrad Hilton Hotel, Chicago, Apr. 24–29, immediately preceding its annual meetings. The course will include sessions on the collagen diseases, pediatric allergy, and emotional factors in allergic disorders; there will be 15 round-table discussions on various aspects of diagnosis and treatment. For full information, address Fred W. Wittich, 401 La Salle Medical Bldg., Minneapolis 2.

The University of Illinois has received a $40,000 gift from Motorola, Inc., for basic research in communications and electronics. Most of the work, in which John Bardeen will be the chief investigator, will be used for research on transistors. Edward C. Jordan will be in charge of projects involving radio and microwave transmission.

McGill University will hold its annual Geography Summer School at Stanstead College, Que., June 29–Aug. 8. Lectures will be given by J. Brian Bird, George B. Cressey, H. C. Darby, Theo L. Hills, Diamond Jenness, L. Dudley Stamp, Bogdan Zaborski, George Jacobsen, Jacques Rousseau, and K. C. Maclure. Three courses on the Arctic, endorsed by the Arctic Institute of North America, extensive field work, and special films of geographical interest will be part of the program. For full information, address Dr. Zaborski at McGill.

Pennsylvania State College will offer a two weeks' seminar July 6–17 for college and secondary school teachers of science on "The Relation of Religion to the Natural Sciences." Wm. G. Pollard, executive director of the Oak Ridge Institute of Nuclear Studies, will direct the study, assisted by visiting scientists and Pennsylvania State staff members. The seminar will be limited to 50 teachers of science with at least three years of teaching experience. Twenty-five scholarships are available. For full information write to the director of summer sessions.

Polytechnic Institute of Brooklyn will hold the tenth of its annual series of summer laboratory courses, June 1–Aug. 7. I. Fankuchen will be in charge of the course on "Industrial Applications of X-Ray Diffraction;" H. F. Mark of "Molecular Weight and Shape of Macromolecules in Solution, including Polyelectrolytes;" and C. G. Overberger of "Progress in Polymerization and Copolymerization Techniques." Dr. Fankuchen, head of the Division of Applied Physics, will supply further information.

Walter Hild, of Hamburg, Germany, is visiting the **University of Texas** Medical Branch for special study in the Tissue Culture Laboratory, and Werner Kunast, also of Hamburg, has been appointed teaching and research fellow in radiology. Molly R. Harrower, consultant in clinical psychology to the Juvenile Courts of the city of New York, is giving a series of lectures and seminars on "Personality Appraisal" Mar. 20–21.

Grants and Fellowships

Applications for appointment as associates for the **University of Michigan** summer symposium on astrophysics will be received until *Apr. 10*. Sponsored by the departments of physics and astronomy, the symposium will run from June 29 through July 24, with the following lecturers: Walter Baade, George Gamow, G. K. Bachelor, and E. E. Salpeter. Advanced graduate students or Ph.D.s who were less than 30 years old on Jan. 1, and who show promise in the area of astrophysics research, are eligible for appointment. The National Science Foundation has provided funds for approximately 15 stipends to cover travel expenses and $200 for living expenses.

The **Purdue Research Foundation** has allocated $90,593 for research fellowships in the Purdue University Graduate School for 1953–54. From these funds, 19 fellowships were established in plant and animal sciences, 9 each in engineering and chemistry, 7 in education and psychology, 4 each in pharmacy and speech, and 3 in mathematics.

The **Social Research Foundation** has awarded $6,000,000 to Yale University for the establishment of the foundation's Fund for Research in Psychiatry, which will provide assistance for basic research in the behavioral sciences to Yale and other universities. The fund will be administered by a Board of Directors, of which Frederick C. Redlich is chairman. Other members are Vernon W. Lippard, Charles D. Aring, John Benjamin, David Shakow, George W. Thorn, and John C. Whitehorn.

In the Laboratories

Armour Research Foundation has appointed Harold M. Coleman, of Armour & Co., and Morgan W. Rider, of the U. S. Rubber Co., Penang, Malaya, assistant supervisors in the Chemistry and Chemical Engineering Department. Frank Lerman, of VioBin Corp., Monticello, Ill., has been named a research chemical engineer.

Stockholders of **Merck & Co.** and **Sharp & Dohme** will vote on a merger agreement at meetings to be held not later than May 5. The combined company will be known as Merck & Co., Inc., but the distinct functions of each firm will be maintained, and the business of Sharp & Dohme continued under its present name. George W. Merck will be chairman of the board, and John S. Zinsser vice-chairman. James J. Kerrigan will be president of the combined company and William L. Dempsey will continue as Sharp & Dohme president.

Schaar and Company, Chicago laboratory equipment and apparatus manufacturers, have received a citation from the Chicago Urban League for outstanding achievement in race relations, as exemplified by the employment of Americans solely with respect to their capacities.

Meetings and Elections

The **Federation of American Societies for Experimental Biology** will hold its annual meeting in Chicago, Apr. 6–10, with the American Society of Biological Chemists as the host society. Scientific sessions and symposia will be held in the Blackstone, Congress, and Conrad Hilton hotels and the Palmer House. The joint session, presenting three papers on the general topic "Some Aspects of Light and Biology," will be held Apr. 7 at the Conrad Hilton, with Vincent du Vigneaud presiding. A special session will be held Apr. 10 in the same hotel, to present a report on the Survey of Physiological Science, with Ralph W. Gerard as chairman.

The **Rumford Bicentennial Symposia and Awards** will be held at the American Academy of Arts and Sciences, Boston, Mar. 27–28. Symposium A, Friday morning, Mar. 27, will deal with "Recent Developments in Thermodynamics," and P. W. Bridgman, Alfred Egerton, Lars Onsager, and Franz E. Simon will speak. Symposium B, on "Recent Developments in Atomic Spectroscopy," will be held Friday afternoon, with Martin Deutsch, Willis E. Lamb, Jr., Edward M. Purcell, and I. I. Rabi as speakers. Friday evening, the Rumford Bicentennial Medals will be presented to Enrico Fermi, Dr. Lamb, and Dr. Onsager. At Symposium C, Saturday morning, Dr. Fermi, J. Robert Oppenheimer, Manne Siegbahn, and Victor F. Weisskopf will discuss "Recent Developments in Nuclear Physics."

Miscellaneous

New journals announced: *Agricultural and Food Chemistry*. Editor, Walter J. Murphy. American Chemical Society, 60 E. 42nd St., New York. Biweekly, scheduled for Apr. 1953. . . . *The Amerindian*. Bimonthly, four-page news bulletin, edited and published by Marion E. Gridley, 27 S. Wabash Ave., Chicago. $2.50 per year. . . . *Circulation Research*. Bimonthly, under the auspices of the American Heart Association. Editor, Carl J. Wiggers, 1775 Broadway, New York. . . . *Diabetes*, a bimonthly, will supplant *Proceedings* of the American Diabetes Association and *Diabetes Abstracts*. Free to members; subscriptions, $9.00 in U. S. and Canada; $10.00 foreign. . . . *Industrial Photography*, 1114 First Ave., New York. . . . *The Journal of the American Geriatrics Society*. Official periodical, edited by Willard Thompson; published by William & Wilkins, Baltimore, Md. . . . *The Journal of Histochemistry and Cytological Chemistry*. Editor, R. D. Lillie. Williams & Wilkins, Baltimore. Bimonthly; $7.50. . . . *The Journal of Rational Mechanics and Analysis*. T. Y. Thomas and C. Truesdell, editors. Graduate Institute for Applied Mathematics, Indiana University, Bloomington. . . . *The Journal of World History*. Quarterly; scheduled for spring 1953. International Commission for a Scientific and Cultural History of Mankind, Unesco, 19 Ave. Kléber, Paris 16e. . . . *Michigan Mathematical Journal*, published

semiannually at the University of Michigan Press, Ann Arbor. $4.00 per year. . . . *Personality: Symposia on Topical Issues.* Editor, Werner Wolff; published by Grune & Stratton, New York. Quarterly; $6.00 per year. . . . *Phytomorphology,* under the auspices of the International Society of Plant Morphologists. Editor, P. Maheshwari. University of Delhi, India. £2, 10s. . . . *Religion and Health.* Monthly; Russell L. Dicks, editor. Duke Station, Box 4802, Durham, N. C. . . . *The Swiss Review of World Affairs,* English translation of articles appearing in *Neue Zürcher Zeitung.* Air mailed monthly from Zurich; subscriptions at University of Chicago Press, $7.00. . . . *Turrialba.* Quarterly. Inter-American Institute of Agricultural Sciences, Turrialba, Costa Rica.

The 12th **Science Talent Search,** sponsored by the Westinghouse Educational Foundation and administered by Science Service, came to an end Mar. 2 with the selection of E. Alan Phillips, 15, of Lincoln, Mass., as winner of the $2800 Grand Science Scholarship. He is the youngest in the 12 competitions ever to win the grand prize. Paul H. Monsky, 16, of Brooklyn Technical High School, placed second. He expects to attend Harvard or Swarthmore, to prepare for a career as a mathematical physicist or mathematician. Alan, who will graduate in June from Weston (Mass.) High School, hopes to prepare for a mathematical career at MIT.

Recent Deaths

Georgi V. Akimov (51), physical chemist, Moscow, Jan. 28; **Walter G. Alexander** (72), physician and civic leader, Orange, N. J., Feb. 5; **Edward L. Aymé** (90), gynecologist and obstetrician, New York, Feb. 3; **Harold Babcock** (66), of Dedham, Mass., ear specialist, Boston, Jan. 21; **Wilder D. Bancroft** (85), chemist, Ithaca, N. Y., Feb. 7; **Nathan Banks** (84), entomologist, Holliston, Mass., Jan. 24; **Henry A. Barrett** (—), radiologist, Warwick, R. I., Feb. 3; **Paul B. Bartlett** (60), economist, Lewiston, Me., Jan. 30; **Gregory P. Baxter** (76), chemist, Cambridge, Mass., Feb. 10; **Theodore M. Berry** (51), electrical engineer, Schenectady, N. Y., Feb. 3; **George W. Biggs, Jr.** (74), civil engineer, New York, Jan. 24; **Miriam L. Bomhard** (—), range conservationist, Glenshaw, Pa., Dec. 16; **Halloran H. Brown** (84), horticulturist, Monsey, N Y., Feb. 1; **J. Thompson Brown** (70), former vice president, E I. du Pont de Nemours & Co., Wilmington, Del., Jan. 31; **Norman Brumbaugh** (68), chemist, Philadelphia, Feb. 15.

Mary S. Case (98), psychologist, South Natick, Mass., Feb. 1; **Arturo Castiglioni** (78), medical historian, Milan, Italy, Jan. 21; **Pedro G. Cofino** (63), agriculturist, Guatemala, Feb. 9; **Thomas J. Courtney** (53), naturalist, Halifax, N. S., Feb. 14; **Jacob D. Cox** (71), industrialist, Cleveland, Feb. 16; **Elijah R. Crossley** (83), eye, ear, nose, and throat specialist, Chicago, Jan. 23; **John B. Delauney** (66), psychologist, Portland, Ore., Feb. 16; **Francis E. Dubois** (77); urologist, Winter Park, Fla., Jan. 31; **Edwin Poe Durrant** (87), physiologist, Columbus, Ohio, Jan. 28; **Lucile Eaves** (84), economist, Brookline, Mass., Jan. 20; **Henry M. Emmons** (75), eye specialist, Boston, Jan. 19; **Julius Ferber** (65), physician, New York, Feb. 6; **Wilfred B. Fetterman** (75), physician, Philadelphia, Jan. 28; **Herbert F. Fraser** (63), economist, Wallingford Hills, Pa., Feb. 9; **Ellis I. Fulmer** (61), biochemist, Ames, Ia., Feb. 10.

Elva A. George (76), of New York, dietitian, Miami, Fla., Jan. 14; **Frank H. Gordon** (74), steel executive, Coatesville, Pa., Feb. 10; **Ilya Grebenshchikov** (66), physicomathematician, Moscow, Feb. 8; **Clarence F. Hale** (75), physicist, Albany, N. Y., Jan. 30; **Isaac F. Harris** (73), biochemist, Rye, N. Y., Jan. 31; **Jacob Heller** (77), obstetrician, New York, Feb. 17; **Joseph A. Hill** (66), chemical engineer, New York, Jan. 15; **Adele S. Jaffa** (84), child psychologist Oakland, Calif., Jan. 20; **Andrew Keogh** (84), bibliographer, New Haven, Conn., Feb. 13; **Abraham Koplowitz** (72), obstetrician and gynecologist, Brooklyn, N. Y., Feb. 19; **C. Austin Kosik** (—), surgeon, New York, Jan. 27; **Oleg Lakhtionov** (—), geologist, Moscow, Feb. 18; **Joseph G. Ludewig** (92), engineer, Rockwell, Md., Feb. 9; **Melvin Maller** (34), of New York, electronics engineer, Riverside, Calif., Jan. 21; **Emil E. Mayer** (68), radio and electrical engineer, New Rochelle, N. Y., Jan. 30; **John V. Mershon** (85), orthodontist, Philadelphia, Feb. 18; **Adolph C. Miller** (87), economist, Washington, D. C., Feb. 11; **Edwin H. Mitchell** (65), electrical engineer, New York, Feb. 5; **Charles Moon** (67), physicist, Washington, D. C., Jan. 31; **Waldo H. Mork** (70), dentist, New York, Feb. 11.

Bernard A. O'Connor (63), of East Orange, N. J., hospital medical director, Newark, N. J., Feb. 15; **Paul L. Parrish** (76), pediatrician, New York, Jan. 29; **Walter B. Pitkin** (74), of Los Altos, Calif., educator, psychologist, and author, Palo Alto, Jan. 25; **William W. Plummer** (75), orthopedic surgeon, Buffalo, N. Y., Feb. 16; **Mikhail B. Plungian** (65), chemist, Fairview Village, Pa., Jan. 29; **Arthur O. Ridgway** (82), engineer, Denver, Jan. 21; **Milo A. J. Roseman** (55), physician, Philadelphia, Jan. 27; **Herbert Schein** (51), psychiatrist, Staten Island, N. Y., Jan. 30; **William S. Schlauch** (79), mathematician, Dumont, N. J., Jan. 27; **Hermann von Schrenk** (79), botanist, St. Louis, Jan. 30; **Robert S. Shaw** (81), educator, East Lansing, Mich., Feb. 7; **Charles F. Sherwin** (68), surgeon, St. Louis, Feb. 12; **Pytor P. Shirshov** (48), hydrobiologist, Moscow, Feb. 19; **Earl L. Shoup** (67), political scientist, Cleveland, Jan. 29; **E. S. Stateler** (62), food chemist, Chicago, Feb. 2; **Herbert Stotesbury** (—), clinical psychologist, Philadelphia, Feb. 16; **Percy R. Turnure** (83), physician, New York, Jan. 23; **Charles M. Waldo** (46), orthodontist, Wellesley, Mass., Jan. 29; **Holburt J. Waring** (87), surgeon, Chepstow, Eng., Feb. 10; **William W. Wells** (51), civil engineer, Portsmouth, Ohio, Feb. 2; **George R. Wieland** (87), paleobotanist, West Haven, Conn., Jan. 18.

Technical Papers

The Influence of X-Irradiation and Atabrine Upon Feathering in the Chick[1]

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Mushett and Siegel (*1*) have described the hematological changes induced by large doses of Atabrine [3-chloro-7-methoxy-9-(1-methyl-4-diethylaminobutylamino)acridine dihydrochloride]. Although they did not observe a leucocytosis in the chicken, this change has been observed in this laboratory (*2*).

In a study designed to investigate modifications of the x-irradiation-induced leucopenia in the chick, it has been observed that feathering is inhibited by irradiation and that this inhibition is overcome by adding Atabrine to the diet.

FIG. 1. Chick on the left received the purified diet supplemented with Atabrine; chick on the right received no Atabrine.

Day-old White Rock chicks were divided into two groups of 15 chicks each and housed in a metal brooder. One group received the purified diet described by Keith *et al.* (*3*), supplemented with 2 mg folic acid/kg of diet. The other group received this same diet plus 500 mg Atabrine dihydrochloride/kg of diet. Food and water were given *ad lib*. After 15 days on the respective diets the chicks were irradiated using the following factors: 15 ma, 220 kv, inherent filtration only, HVL 0.25 mm Cu, 32 in. to the center of the animal, 20.4 min at a rate of 42.5 r/min to a total of 865 r (in air), field size covering entire chick.

[1] Research paper No. 981, Journal Series, University of Arkansas. This work was supported in part by a contract with the Atomic Energy Commission and a grant from the National Institutes of Health, USPHS.

The average initial weights, as well as the average rate of weight gain of the chicks over the experimental period, were equal.

The chicks were photographed 26 days after irradiation, one bird from each group being selected at random for each photograph. At approximately 15 days after irradiation it was observed that the chicks that had received Atabrine were feathering at a faster rate than those not receiving Atabrine. The birds that had not received Atabrine produced apparently normal wing and tail feathers, but they developed very few feathers on the breast, back, and neck (Fig. 1).

Further studies are in progress and will be reported at a later date.

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Does Phosphorylated Hesperidin Affect Fertility?[1]

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Phosphorylated hesperidin, a hyaluronidase inhibitor (*1*), has recently been reported by several investigators to act as a new antifertility factor when administered either orally or intraperitoneally to the rat (*2*), mouse, and human (*3*). Since it is claimed that this substance may be used orally in both males and females, such an important discovery deserves further critical verification. Moreover, if this substance has an effect on fertility, it is of importance to determine whether this is due to the inhibition of sperm penetration into the eggs, as interpreted by these investigators, or whether it is due to the inhibition of ovulation, of the physiological functions of the germ cells, or of implantation and normal development of the embryo. Adult rats and rabbits were used in the present experiments to evaluate these possibilities.

The following two series of tests were performed on rabbits:

a) In order to determine whether phosphorylated hesperidin inhibits fertilization, a doe was bred twice by fertile bucks and 10½–11 hr later, at the time when pene-

[1] This work was supported by grants from the Dickinson Memorial Fund of the Planned Parenthood Federation and from Rockefeller Foundation. Sincere thanks are due to G. J. Martin, of the National Drug Company, Philadelphia, for supplying phosphorylated hesperidin, and Elizabeth M. Hull for assistance.

tration of sperm into the eggs normally occurs, .03 ml 1% phosphorylated hesperidin in saline was deposited via the fimbria into the ampulla of each Fallopian tube. The animal was sacrificed 24 hr after operation, and the eggs were recovered, fixed, stained, and examined to determine whether they were fertilized (*4*).

b) In order to investigate the possibility that phosphorylated hesperidin inhibits the functional activity of spermatozoa, semen collected with an artificial vagina was suspended in saline containing different concentrations of phosphorylated hesperidin. A 0.5 ml aliquot (containing 5–8 million spermatozoa) of one of these suspensions was deposited in the vagina of female rabbits, and pituitary extract was injected intravenously to induce ovulation. The animals were sacrificed 24 hr later, and the eggs were recovered, fixed, stained, and examined. The results of these two series of tests are presented in Table 1.

TABLE 1

FERTILIZATION OF RABBIT EGGS

	Concentration (%)	Rabbit	No. of eggs	Eggs fertilized (%)	Condition of fertilized eggs
Deposition of phosphorylated hesperidin into the tubes	1	1	15	100	4–8 Cell stage
		2	9	100	
		3	4	100	
		4	13	100	
Insemination of sperms suspended in phosphorylated hesperidin	1	5	7	0	Pronuclear, or 2-cell, stage
		6	13	15	
		7	3	0	
		8	11	55	
	.1	9*	55	42	Pronuclear, or 2-cell, stage
		10	11	36	
		11	11	100	
		12	11	64	

* Superovulated.

Two experiments were performed on rats in the following manner. (The dosage used was approximately the same as stated by previous investigators (*2, 3*)—i.e., 20 mg/kg intraperitoneally and 100 mg/kg orally.)

a) Ten females, of 200–250 g body weight, and 6 males of proved fertility were each injected intraperitoneally daily for 6 days with 5 mg of phosphorylated hesperidin in saline. Then two groups of 5 females and 3 males were put together in separate cages, and injections were continued until the females were killed.

b) Another 11 females and 6 males were hand-fed daily with 20 mg of phosphorylated hesperidin in 0.5 ml of saline. Six days later, 5 females and 3 males were put together in one cage, and 6 females and 3 males in another cage. After two weeks of hand-feeding, in order to avoid further emotional disturbance of the animals, 20 mg of phosphorylated hesperidin was dissolved in 10 ml of water and served as drinking water daily for each animal until the end of the experiment.

In both experiments, the animals were killed either when pregnancy was assured by palpation or 27 days after the beginning of the experiment. The numbers of corpora lutea and those of normal and degenerated embryos were recorded. The ages of the embryos were determined by their size in order to estimate the time of conception. The results of these two tests and data collected in control animals are presented in Table 2.

TABLE 2

PREGNANCY OF RATS

	No. of female rats		Av time interval between cohabitation and conception (days)	Av no. of corpora lutea	Av no. of normal embryos	Av no. of degenerated embryos
	Not pregnant	Pregnant				
Intraperitoneal injection of phosphorylated hesperidin (5 mg/rat/day)	0	10	5.4	13.6	10.9	.5
Oral administration of phosphorylated hesperidin (20 mg/rat/day)	2	9	4.5	12.5	10.5	.33
Control	0	9	5.2	8.7	6.4	.2

From the results of this study, it is quite clear that phosphorylated hesperidin does not inhibit fertilization when deposited into the Fallopian tubes of rabbits at the time of sperm penetration, nor does it inhibit ovulation, implantation, or normal development of the embryo when administered intraperitoneally or orally to rats. Although the motility was unaffected, however, the fertilizing capacity of rabbit sperm appeared to be inhibited to a certain extent when the sperm was suspended in a 1% solution of phosphorylated hesperidin. That such a concentration of phosphorylated hesperidin could reach the testis or epididymis of an animal when administered orally or intraperitoneally is very doubtful. It should be mentioned here that, although a 1% solution of phosphorylated hesperidin can inhibit the fertilizing capacity of the spermatozoa *in vitro*, it does not inhibit fertilization or even the fertilizing capacity of the spermatozoa *in vivo* when deposited into the tubes.

Since there is so great a discrepancy between the results obtained in the present study and those reported by previous workers, it was thought that the potency of the phosphorylated hesperidin as a hyaluronidase inhibitor should be determined. Therefore, one group of rabbit eggs in mucous clots, recovered 10½ hr after a sterile mating, was placed in a watch glass containing 1 ml of a 0.01% solution of phosphorylated hesperidin in saline, and another group in one

containing saline alone. Then .05 ml of undiluted rabbit semen was added to each watch glass. Periodic observation revealed that the dispersal of the cumulus clot took 10 min in the saline solution, and ½–1 hr in the phosphorylated hesperidin. Therefore, the phosphorylated hesperidin used in the present study was undoubtedly potent as a hyaluronidase inhibitor, but its potency is relatively weak as compared with nitrated hyaluronic acid (*5*) in the inhibition of follicular cell dispersal and in the inhibition of the fertilizing capacity of spermatozoa.

Our knowledge of the actual function of sperm hyaluronidase in fertilization is as yet obscure, but we do know that one of its functions is the dispersal of follicular cells surrounding the egg. However, since it has been shown by several investigators that follicular cell dispersal is not a prerequisite of sperm penetration into the eggs (*6*), a hyaluronidase inhibitor would not necessarily be a fertilization inhibitor.

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The Natural Concentration of Deuterium in Honey[1]

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In the early 1930s, when heavy hydrogen excited the interest of scientists, extensive studies were carried out with the application of deuterium to biological systems.

The enthusiasm resulted in interesting findings by Hevesy, Schoenheimer, Rittenberg, Dole, Washburn, DeWitt-Stetten, and others, yet many problems were left unsolved and many phenomena unexplained.

It has been found that living organisms will tolerate only to a certain limit the exchange of the water in the body to the chemically identical deuterium oxide. Experiments on this problem resulted in the hypothesis that deuterium, having a different resonance, or exchange potential, from hydrogen toward certain bonds of intermediate metabolites, will interfere with the proper work of the donors or acceptors, as well as other enzyme systems essential for the maintenance of life. In accordance with this theory some of the data indicate that living tissues have a tendency to accumulate deuterium to a limited degree.

The appearance of deuterium in tissues can be easily explained by the uptake of natural water, which contains in general about 1 part of the isotope in 5000 parts (*1*) or, more precisely, 0.0147 mol% D (*2*). But further work is necessary to explain, for example, why the sap of a willow tree is significantly richer in deuterium and why the wood has an increment double that of sap (*1*). Since the vapor pressure of deuterium oxide is about 7% below that of water (*2*), it is possible that through transpiration plants are acting as a still and that by fractioned distillation of large quantities of water they might accumulate deuterium oxide in their tissues.

It is known that hydrogen of the OH-groups in glycogen or sugars can be exchanged for deuterium (*3*) if the latter is in abundance in the environment, but this process is slow (*4*) and would hardly account for the excess of deuterium in metabolites. A more likely theory is that deuterium enters into metabolic processes and becomes bound to carbon atoms (*5*); hence the increment as reported, for instance, in honey (*6*).

Little is known about the physiological effect of deuterium, but since it does interfere with metabolism and it is built into carbohydrate molecules, it is available to every cell or tissue through anabolic reactions. Beyond the known physiological action of deuterium, there might be a long-range effect reaching into the realm of genetics, or the theories of neoplasts.

Density measurements for the determination of the deuterium content were carried out with the falling-drop (*7, 8*) or the totally immersed float method (*9, 10*) or with the Cartesian diver. These methods are very sensitive, yet from many points of view it is more convenient to use a mass spectrometer (*11*).

It was of interest to repeat the experiments with honey, extending them to separate determinations of the deuterium ratio in the moisture and the sugars of honey. The material used was a *1951* buckwheat honey from the Finger Lakes region, with a moisture content of 17.9%. The following samples were analyzed:

Sample M: The somewhat crystallized honey was dehydrated at room temperature, and the moisture trapped in a cooling mixture of acetone–solid carbon dioxide. The condensed liquid was extracted with ether to eliminate volatile metabolites, then the total amount was redistilled to avoid fractionation of deuterium oxide.

Sample M_2: To eliminate crystal water, the dry honey was heated slowly under normal pressure until the first signs of caramelization. This residual water was condensed and passed through a combustion tube.

Sample S: The slightly caramelized honey was combusted with oxygen and a platinum sponge. The condensed water was recombusted to eliminate all traces of organic matter.

Sample D: The crystals of the honey, mainly dextrose, were separated by vacuum filtration and washed with absolute methyl alcohol.

Sample L: The honey which passed through the Buchner funnel was dried *in vacuo*. It contained 36% more levulose than dextrose. Samples D and L were combusted as described for Sample S.

For the measurements in the mass spectrometer,

[1] This work was supported by a grant from the Dyce-Processed Honey Fund, Department of Entomology, Cornell University.

about 0.1 ml of the sample was placed in a small platinum container in a combustion oven. The vapor passed through zinc, heated just below its melting point. The resulting hydrogen and deuterium were accumulated in a sampler and fed through a manifold into the tube of the spectrometer. The resulting data on mass 3/mass 2—that is HD/H_2—were converted into the excess in mole % deuterium. The averages of the results are shown in Table 1. The results indicate

TABLE 1

Sample	Excess (mole % D)	Increment (% D)
M	0.0025	17
M_2	.0025	17
S	.0041	28
D	.0031	21
L	.0044	30
Wax	0.0028	19

that the natural abundance of deuterium in honey, as determined through densimetric measurements by Dole (*6*), seems to be verified by these mass spectrometer data. The error in the measurements with the mass spectrometer is in general below ± 5%.

The differences in the various samples are distinct, and, compared with the average of deuterium in rain and lake water, as given by Bleakney and others (*12, 2*), they are significant.

The values obtained in this table are based upon our standard containing 0.0148 mole% D, and we can assume that buckwheat plants in the Finger Lakes region have taken up water with the same average deuterium content.

The increment of the isotope deuterium in Sample M might indicate that the moisture in the nectar of flowers is coming partially from anabolic degradation of sugars, and is probably enriched through repetitive processes.

The fact that honey contains more levulose than dextrose, and that the levulose has in this sample about two times higher deuterium content, could point to a specific deuterium affinity of the invertase in the stomach of the bees, which could build deuterium atoms into sugar molecules at some point in the hydrolytic process. There are a few indications in the literature that deuterium has an influence on enzymatic systems (*13*): inhibitory action at higher concentrations (*14*), stimulating at low concentrations (*15*), even raising the resistance of certain bacteria toward strong disinfectants (*16*).

It should be mentioned that the dispersion coefficient—namely, $\frac{\text{mass 3/mass 2 in sugar}}{\text{mass 3/mass 2 in water}}$—is quite negligible by such low concentrations as it is present in living tissues, and the dispersion coefficient of fructose, which is about 10% higher than that of glucose (*17*), cannot account for the excess of deuterium as found in our experiments.

These data and the preliminary conclusions drawn need, of course, further work and confirmation. Besides the repetition of above experiments with other honey samples it would be interesting to have the data on the water from the geographical micro-unit where the honey was gathered; it would also be important to feed plants with excess heavy water and analyze the nectar for its deuterium content, or feed the bees with deuterium oxide and determine the deuterium in the sugars of the honey produced by them. Beyond the apicultural significance of this question it is enormously interesting for our general concept of biochemical reactions.

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Competitive Action of Isonicotinic Acid Hydrazide and Pyridoxal in the Amino Acid Decarboxylation of *Escherichia coli*

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We have previously shown that the inhibitory effect of isonicotinic acid hydrazide (INAH) on the growth of *Escherichia coli* significantly decreases in broth media (more than 10 mg/ml), compared with that of INAH (0.6–1.2 mg/ml), in a synthetic medium (Anderson's *M*-9 medium) (*1, 2*).

Thus it is possible to postulate the existence of certain substances that may be contained in broth and that are able to inhibit the action of INAH on the growth of *E. coli*. In further investigations of these postulated substances, we found that one of them can, to some extent, be replaced by pyridoxine hydrochloride (*1, 3, 4*); hence, it may be suggested that there is an intimate connection between INAH and pyriodoxine and its derivatives.

It has been generally agreed that pyridoxine derivatives play an important part in some enzyme systems of *E. coli*—i.e., decarboxylase (*5, 6*), tryptophanase

[1] We express our thanks to Dr. Egami, of the Department of Biochemistry, Nagoya University, for his kind advice.

(7), and transaminase (8, 9)—as their cofactor. Therefore it is not impossible to predict the inhibitory effect of INAH and also the competitive effect of pyridoxine and its derivatives on INAH in these enzyme systems.

While attempting to investigate the action of INAH on the amino acid (arginine, orithine, and glutamic acid, etc.) decarboxylating activity of washed suspensions of *E. coli*, evidence has been obtained that the cell suspension treated with INAH remarkably decreases its decarboxylating activity, more or less in proportion to the amounts of INAH added, and that the activity recovers when pyridoxal is added to the reaction system. Typical results showing the effect of INAH on the arginine decarboxylating activity of *E. coli* communior (stock) are given in Fig. 1 (Expt. 1); the results showing the recovery effect of pyridoxine and pyriodoxal are given in Table 1 (Expt. 2).

In order to obtain the activity of arginine decarboxylation, a culture of *E. coli* communior (stock) was grown at 25° C in 2% glucose broth containing 10 mg/liter of arginine for 16 hr (*10, 11*). At the end of the incubation period the organism was centrifuged out of the growth medium, washed in saline three times, and then made up into suspension in McIlvaine's citric acid–phosphate (pH 4.2) buffer (*12*). The dry weight of organism/ml suspension was determined in each case by a photoelectric nephelometer.

The evolution of CO_2 from arginine under the action of washed organisms in suspension was studied in a Warburg manometer. The following quantities were used: In Expt. 1, in the main compartment of the flasks, 0.5 ml washed suspension; 0.6 ml of 0.1 *M*, 0.3 ml of 0.1 *M*, 0.05 *M*, 0.025 *M*, and 0.0125 *M* INAH, respectively, and in the side bulb, 0.5 ml *M*/30 solution of arginine; in Expt. 2, in the main compartment of the flasks, 0.5 ml washed suspension, 0.3 ml of 0.1 *M* INAH, and in the side bulb, 0.3 ml of 0.1 *M* pyridoxine hydrochloride and pyridoxal hydrochloride, respectively, 0.5 ml *M*/30 solution of arginine.

The quantity of the liquid in the flask was then made up to a volume of 3.0 ml with McIlvaine's citric acid (0.1 *M*)-phosphate (0.2 *M*) buffer (pH 4.2) in each experiment. The gas phase was air. In order to obtain the effective action of INAH on the cell suspension, these flasks were agitated at 37.5° C without reagents for 30 min, and then the reagents in the side bulb were instantaneously mixed in each main compartment. The experiments were run at 37.5° C, and the gas output during the first 5 min was disregarded.

The *Q* values were calculated as follows:

$$Q_{CO_2}^{air} = \left(\begin{matrix}X_{CO_2}\text{ evolved in}\\ \text{experimental flask}\end{matrix}\right) - \left(\begin{matrix}X_{CO_2}\text{ in correspond-}\\ \text{ing control flask}\end{matrix}\right)/\text{dry weight of cell (mg)/hr}$$

As may be observed in Fig. 1 from the results of Expt. 1, INAH considerably, though not completely, inhibits the arginine decarboxylase activity of the washed coli-cell suspension, and the inhibitory effect of various amounts of INAH is as follows:

Final conc of INAH (*M*/liter)	Inhibitory effect (%)
0.02	70
.01	65
.005	47
.0025	34
0.00125	12

From the results of Expt. 2 (Table 1), it will be seen that pyridoxal (final conc, 0.01 *M*) recovers the arginine decarboxylase activity of the washed suspension inhibited with 0.01 *M* (final conc) INAH by more than 60% for the first 30 min.

Therefore, considering that the coenzyme of amino acid decarboxylase has been determined as pyridoxal-

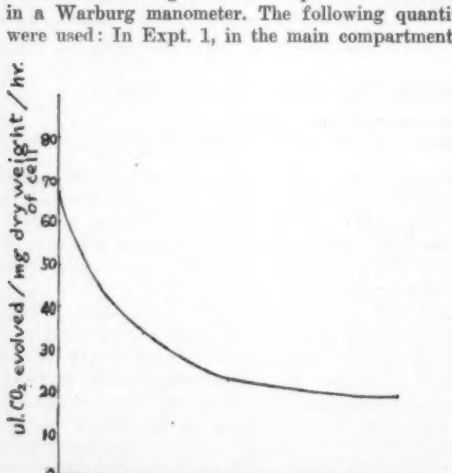

FIG. 1. Expt. 1: Inhibitory activity of INAH on the arginine decarboxylase of the washed suspension of *E. coli* communior (stock). Temp, 37.5° C; substrate, *M*/180 arginine (final conc); INAH was in contact with the washed suspension of cell at 37.5° C for 30 min.

TABLE 1

RECOVERY EFFECT OF PYRIDOXINE AND PYRIDOXAL*

(Experiment 2)

No.	Final conc INAH (*M*/liter)	Substance added	Q_{CO_2}/mg dry wt of bacteria cell	Recovery effect (%)
1	0.01	—	20.5	—
2	0.01	Pyridoxine (0.01 *M*)	30.5	20.0
3	0.01	Pyridoxal (0.01 *M*)	51.0	63.0
4	—	—	70.5	—

* Temp., 37.5° C; substrate, *M*/180 arginine (final conc); pyridoxine and pyridoxal were added, respectively, at the end of INAH-contact with cell. Recovery percentage was calculated from the following equation:

Recovery percentage = $[Q_{CO_2}\ (2 \text{ or } 3-1)/Q_{CO_2}\ (4-1)] \times 100$.

5-phosphate, these results indicate that the substantial recovery effect by pyridoxal is due to its competitive activity on INAH. Whatever the mode of the competitive action of INAH and pyridoxine derivatives may be, one important implication of these experiments is that INAH can act on amino acid decarboxylase of *E. coli* as an inhibitor, possibly being an antimetabolite against pyridoxine derivatives. These results are consistent with those obtained in experiments on the inhibitory action of INAH on the indole formation of *E. coli* (*4*).

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Determination of Specific Activities of Tritium-labeled Compounds with Liquid Scintillators

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Recently several articles (*1–4*) have appeared on the determination of specific activity of compounds labeled with low energy β-emitting isotopes using liquid scintillation techniques. This procedure, which provides both ideal geometrical conditions and a relatively rapid technique of measurement, consists of dissolving and counting the labeled material in a liquid scintillator, such as terphenyl-xylene, terphenyl-dioxane, or 2,5-diphenyloxazole-toluene.

The following communication describes preliminary results obtained from the measurement of tritium-labeled materials using liquid scintillators and an experimental arrangement which permits satisfactory counting efficiency. The method may be applied to counting both tritium-labeled organic and inorganic compounds.

In general, present techniques for the determination of tritium are experimentally involved, especially for an organic material. Briefly, these methods are:

1) Ionization chamber measurement of hydrogen gas obtained by the combustion of sample to water and reduction of this water to hydrogen (*5*).

[1] We are pleased to acknowledge the aid of Winifred Bennett and Richard Cotton for the ionization chamber analyses and of Alice McCarthy for the preparation of the scintillation solutions.

2) Geiger tube measurement of a tritiated hydrocarbon obtained by the combustion of sample to water and reaction of water with Grignard reagent (*6*) to give tritiated hydrocarbon.

3) Measurement of solid samples with windowless, methane-flow-type counter operated in the proportional region (*7*).

TABLE 1

Counting of Tritium-labeled Compounds Using Liquid Scintillators

Compound	Liquid scintillator	Expected cps from ionization chamber analysis	Measured cps from scintillation analysis*	Counting efficiency for scintillation method
Tritiated stilbene	Phenylcyclohexane, diphenylhexatriene, terphenyl	10,650	790	7.4%
Tritiated water	Dioxane, terphenyl	10,000	380	3.8%

* Average of several readings.

The two methods employing gas counting have high efficiencies (70–100%) but involve quite complicated preparation techniques; and that using solid samples, although simple, has fairly low counting efficiencies (~2–3%).

The tritium-labeled materials that we have counted are approximately 3% by weight of tritiated water in a solution of dioxane containing 5 g/liter of terphenyl and tritiated stilbene (*8*) in a solution of phenylcyclohexane containing 3 g/liter of terphenyl and .01 g/liter of diphenylhexatriene (*9*). The *p*-dioxane was purified by distillation over sodium at atmospheric pressure, and the phenylcyclohexane was distilled at reduced pressure through a fractionating column.

The experimental arrangement used for this set of measurements was similar to that described in a previous article (*3*), and all data were taken at room temperature. However, here the integrating time constant at the output of the photomultiplier tube was 1 μsec. Because of significant phosphorescence of the liquid scintillators, all solutions were allowed to dark-adapt for at least 30 min before a measurement was taken.

The preliminary results thus far obtained are summarized in Table 1. The ionization chamber analyses were accomplished by combustion of the stilbene on a semimicro scale and conversion of the tritiated water to hydrogen gas (*5*), which was then counted in an ionization chamber with a Lindemann-Ryerson electrometer (*10*). The equivalence of rate of discharge of the electrometer (mv/sec) per millicurie of tritium gas was established with aliquots of tritium obtained by manometric dilution of several tritium ampules of given activity, as supplied by Oak Ridge National Laboratory.

The scintillation measurements were taken in the form of integral bias curves with the photomultiplier tube at a fixed voltage (hv = 1320 v). The reported counting rates were obtained by extrapolating the integral bias curves to zero pulse height. The difference in counting efficiency for the two tritiated compounds investigated is explainable in terms of the larger pulse height obtained with the phenylcyclohexane solution than with the dioxane solution, the former yielding light pulses about twice as large as the latter. Since light pulses produced in the liquid scintillators by the tritium β-particles (av energy = 5.69 kev [*11*]) are so small, the counting efficiency might be expected to be proportional to the average pulse height over a limited region. Rough analysis and comparison of the integral bias data in terms of average pulse height for both the tritium β and an external Sr^{90} β-source give an average energy for the tritium β that is much too large. The reason for this discrepancy is not apparent at this time, but work is in progress to rationalize this point. From consideration of the data obtained it would appear that the discrepancy cannot be explained in terms of multiple counting but may involve the statistics associated with the emission of 1 or 2 photoelectrons/β-particle from the photomultiplier tube.

From consideration of the preliminary results obtained, it would appear that counting of tritiated compounds of high specific activity with liquid scintillators would offer a valuable, complementary method to gas counting. Liquid scintillators would appear to fulfill a role similar to that provided by flow-counting of solids; although neither of these two methods provides the high efficiency obtainable in gas counting, they have the important advantage of allowing easier and more straightforward sample preparation. However, it should be noted that the scintillation technique has an increased advantage over solid-sample counting in that it provides significantly higher efficiencies. With improved electronics, particularly employing photomultiplier tubes of higher photocathode sensitivity, much higher counting efficiencies should be obtainable.

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Direct Effect of X-Rays on Bacterial Viruses, Modified by Physical State, in Relation to the Target Theory[1]

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Experimentation involving the target or hit theory must distinguish clearly between direct and indirect effects. The general assumption has been that x-ray inactivation of bacterial viruses in a proteinaceous medium or in a dried condition is due to direct effects of the radiation. The results here reported consider an aspect hitherto little considered, namely, the effect of the physical condition of dry phage particles on their resistance to x-irradiation. Bacteriophage T1, specific for *Escherichia coli*, strain B, was irradiated with unfiltered 50 kv x-rays in a special device (*1*) at various temperatures. The experiments utilized lyophilized phage in broth and vacuum-dried phage in broth. To insure inactivation from what has been considered direct effect only, three precautions were taken: the viruses were suspended in broth, thereby assuring a protective medium; they were vacuum-dried for 24 hr, or lyophilized and stored in a vacuum desiccator for 24 hr, thereby assuring a minimum of free water; they were irradiated *in vacuo*, thereby assuring a minimum of oxygen and moisture at the time of irradiation.

No inactivation caused by temperature alone was observed at temperatures below 310°K, although the effect of temperature at the time of irradiation is considerable. This remarkable effect of temperature will be reported in greater detail elsewhere. The emphasis is here placed on the difference in the effectiveness of x-rays on viruses which have been dried differently, but in all other respects treated exactly the same.

On the assumptions of the target theory, one would expect that the ionization would be equally effective in inactivating the virus, whether it was vacuum- or freeze-dried, since all other physical conditions were kept constant. Table 1 shows, however, that the survival after irradiation is considerably higher for T1 vacuum-dried than for T1 lyophilized, and this remains consistent even when the temperature of the irradiated material is varied over wide ranges. It is noteworthy that Groups III and IV in Table 1 show the same degree of x-ray sensitivity. This fact prevents a postulate claiming that the difference of effectiveness of x-rays with the two methods of drying was due to the cumulative effect of damage initiated by the lyophilization process, which is either lacking or not so pronounced in the vacuum-drying process. The two samples of lyophilized material from the same stock culture

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TABLE 1

SURVIVAL OF VACUUM-DRIED AND LYOPHILIZED T1 BACTERIOPHAGE AFTER X-IRRADIATION*

	Av titer (particles/ml)			
	T1 vacuum-dried		T1 lyophilized	
	Group I	Group II	Group III	Group IV
Nonirradiated controls	3.01×10^9	3.69×10^9	1.73×10^9	3.87×10^9
216,000 r at 77° K	2.01×10^9	2.39×10^9	5.98×10^8	1.20×10^9
216,000 r at 194° K	1.77×10^9	1.91×10^9	4.18×10^8	9.36×10^8
216,000 r at 310° K	1.28×10^9	1.51×10^9	2.36×10^8	5.77×10^8
	Fraction surviving (N/N_o)			
Nonirradiated controls	1.000	1.000	1.000	1.000
216,000 r at 77° K	0.668	0.648	0.346	0.310
216,000 r at 194° K	0.588	0.518	0.241	0.242
216,000 r at 310° K	0.425	0.409	0.136	0.149

* The same stock of viruses was suspended in 0.8% nutrient broth, and either vacuum-dried or lyophilized. Irradiations were performed at temperatures of 77° K, 194° K, and 310° K, with 216,000 r N/N_o = fraction of active phage after irradiation. Data are based on 54 samples, 290 Petri plates, and 58,000 plaques.

show a marked difference in degree of lyophilization damage, but do not, however, show any essential difference in sensitivity to x-rays, since the fraction surviving x-rays (N/N_o) is essentially the same for both lyophilized groups.

Table 2 contains some physical values, commonly deduced from the irradiation of viruses, based on Table 1. The spread of values obtained by varying temperature and the drying process is significant. The effects of these two factors, previously assumed to be of negligible importance when dealing with direct effects of ionizing radiations (*2*), are evident in the table. Hits per phage are calculated from the Poisson distribution formula for the dose used, 216,000 r. The inactivation dose is that which reduces the surviving phage to 37% (e^{-1}) of the initial amount. The calculations of target size in the second part of Table 2 are based on the commonly used method, which assumes that the ionizations are produced in the phage particles singly and at random. In the event that the target dimensions are greater than the separation of consecutive ionizations, the dose required for a given inactivation is proportionately greater than allowed for by this method of calculation, and the target size is underestimated. This appears to be the case, as shown in the third part of Table 2, in which the target size is calculated according to the method elaborated by Lea (*2*), called the associated volume method. This method of calculation takes into consideration the relative target size, the density of the irradiated material, and the spatial distribution of ionizations, the latter being related to the wavelengths of the x-rays. This prevents underestimation of target size. The differences in the physical values obtained from the irradiation of dried phage and from the irradiation of lyophilized phage are even greater when based on this newer method of calculation.

TABLE 2

PHYSICAL VALUES DEDUCED FROM DATA IN TABLE 1

	T1 vacuum-dried and irradiated at			T1 lyophilized and irradiated at		
	77° K	194° K	310° K	77° K	194° K	310° K
Hits per phage at 216 kr	0.42	0.59	0.87	1.11	1.42	1.94
Inactivation dose (kr)	517	365	247	194	152	111
	On basis of random distribution of single ionizations					
Target size (10^{-18} cm^3)	0.97	1.37	2.02	2.58	3.28	4.51
Phage vol/sensitive vol	61.3	43.2	29.3	22.9	18.0	13.1
Ionic yield	0.016	0.023	0.034	0.043	0.055	0.076
	On basis of associated volume method of Lea					
Target size (10^{-18} cm^3)	3.54	6.28	8.98	12.4	16.7	25.2
Phage vol/sensitive vol	16.7	9.43	6.59	4.78	3.55	2.35
Ionic yield	0.06	0.11	0.15	0.21	0.28	0.43

The ratio of dry phage volume to sensitive volume indicates the relative portion of the dry phage particle which is insensitive to x-rays. The ionic yield, M/N, is the number of molecules of a specific substance formed or destroyed per ion-pair produced. Applied to the inactivation of bacteriophage, it represents the efficiency of the x-rays in producing inactivation. Our values encompass the single value given by Watson (*3*) for other viruses.

These discrepancies are of considerable importance

in considerations of the target theory, insofar as they involve what appears to be the direct action of ionizing radiations. To date some consideration has been given to temperature (*4, 5*), but apparently no one has considered vacuum-dried material *vs.* freeze-dried material from the viewpoint of direct effects of ionizing radiations.

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Studies on Uracil Utilization in Normal and Acetaminofluorene-treated Rats[1]

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Although there have been several recent reports of studies of uracil metabolism in lower organisms (*1, 2*), it has been generally assumed, on the basis of isotopic N^{15} studies (*3, 4*) that higher organisms cannot utilize exogenous pyrimidines for nucleic acid synthesis. Data reported recently from this laboratory (*5*), however, indicating that uracil reverses the inhibitory effect of thiouracil on the development of hepatoma in acetaminofluorene (AAF)-treated rats, suggested that the metabolism of uracil in this species may be altered under these circumstances.

Experiments were undertaken to test the possibility that uracil serves as a nutritional factor for tumor tissues. The preliminary results of these experiments demonstrate that, in contrast to normal liver, AAF-induced hepatoma tissue incorporates exogenous C^{14}-uracil into its nucleic acids (*6*) and, further, that the general metabolism of this pyrimidine is slightly accelerated in the tumor-bearing animal.

In a typical experiment, reported here, 20 mg 2-C^{14}-uracil,[4] containing 4×10^6 cpm, was injected intraperitoneally in the test animals (Wistar strain male rats, 300–350 g), normal and tumor-bearing (Table 1). The purity of the labeled compound was established by butanol-H_2O chromatography on paper (*7*); the eluted spot corresponded in R_F to recorded values and contained 95% of the anticipated radioactivity. The animals were sacrificed 3 hr after injection, respiratory CO_2 and total urine being collected during the experimental period. The liver (or hepatoma) was immediately homogenized in cold trichloracetic, and the nucleic acid was obtained from the lipid-free nucleoprotein by the Schneider procedure (*8*). The nucleic acids were freed of TCA by a combination of boiling and ether extraction, and assayed by direct plating. After assay the crude nucleic acids were hydrolyzed in HCl for 1 hr and subjected to ion exchange chromatography on a Dowex 1 formate column (*9*). The acid-soluble activity of the liver was assayed directly after ether extraction of the precipitant. Radioactivity of plasma and urine was determined on dried untreated aliquots of these materials; the respiratory C^{14} was assayed as $BaCO_3$. After extraction of the nucleic acids, the proteins were dissolved in 2 *N* KOH, reprecipitated and assayed by direct plating after solvent dehydration.

The gross distribution of radioactivty and that exhibited by liver components are shown in Table 1. Rapid catabolism of the uracil and excretion of the isotope occur in both normal and tumor-bearing rats, but are somewhat accelerated in the latter. The activity of the ureido-carbon in both normal and tumor-bearing animals requires further evaluation in relation to the formulation of urea as the major end product of pyrimidine metabolism (*10*).

In contrast to the relative inertness of uracil in normal rats, these data reveal considerable incorporation of the isotope into the hepatoma nucleic acids, paralleled by an increased isotope content in the acid-soluble constituents. The levels of isotope in the purified proteins suggest that the recycling of C^{14} may be due

TABLE 1

DISTRIBUTION OF URACIL C^{14} RADIOACTIVITY

	Normal rat*	Tumor-bearing rat†
	(% of dose)	
Respiratory CO_2	23	46
Urinary C^{14}	25	33
Total liver	0.1	2.2
Plasma	0.1	0.05
(extracellular water)	12	5‡
	Normal liver	*Hepatoma*
Acid-soluble§ (cpm)	3200	75,000
Crude nucleic acids (cpm/mg)	5.0	40
Protein (cpm/mg)	2.0	3.0

* Stock diet.

† 0.03% AAF incorporated in the stock diet; animal sacrificed after 10 months; frank hepatoma present.

‡ Based on 55% of body weight, assuming equilibration at the isotope level of the plasma.

§ C^{14} content/whole liver supernatant.

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[2] In partial fulfillment of the requirements for the Ph.D. degree in biochemistry.

[3] We wish to acknowledge the excellent technical assistance of Edith Gollub.

[4] Synthesis of the C^{14}-uracil was carried out by Charles Miller, of Sharp & Dohme, North Wales, Pa., using C^{14}-urea supplied by Technical Associates, Glendale, Calif., under authorization by the AEC. We wish to express our grateful thanks to Dr. Miller and to Lemuel Wright, of Sharp & Dohme, for this assistance. We also wish to express thanks to Howard E. Skipper, of the Southern Research Institute, whose gift of labeled uracil made initial experiments possible.

to CO_2 fixation. This incorporation, conceivably by direct CO_2 fixation (*11*) or via pyrimidine precursors such as aspartic acid (*12*) and lactic acid (*13*), may be adequate to explain the isotope content of the nucleic acids of the normal liver but not of the hepatoma.

The conclusion that the uracil has entered into nucleotide formation is supported by the results of ion exchange fractionation. The Dowex I formate forecuts, containing the impure purine bases, exhibited activities of *ca.* 10–15 cpm/mg of base, whereas the activity of the main cytidylic and uridylic acid fractions was 170 and 230 cpm/mg of base, respectively. The absence of uptake into the purine bases and the approximate correspondence between observed pyrimidine nucleotide isotope content and that expected (*ca.* 250 cpm/mg base) on the basis of nucleic acid specific activity suggest a reasonably direct utilization of the uracil. The significance of the radioactivity present in other fractions awaits further purification.

On the basis of the detailed experiment reported, as well as of a number of preliminary tests, it appears probable that AAF carcinogenesis involves an alteration of the pattern of nucleic acid metabolism of the liver, one aspect of which involves the utilization of preformed uracil. Although the basic significance of this observation remains to be established, it appears likely that this metabolic alteration underlies the striking ability of thiouracil to inhibit hepatoma formation by AAF. The work of Kidder *et al.* (*14*) indicates that another nucleic acid antagonist, 8-azaguanine, depends for its inhibitory action (in *Tetrahymena geleii*) on the physiological state of the test organism.

Studies are in progress to determine whether the altered metabolism observed in the hepatoma is shared by other growing systems such as regenerating liver and embryonic tissues. The rapid catabolism of uracil has also indicated the desirability of investigating possible exchange reactions around the ureido carbon.

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Comments and Communications

Development of Strains of Albino Mice with Predictable Susceptibilities to Audiogenic Seizures[1]

Laboratory mice have some advantages over rats for the study of audiogenic seizures. The level of incidence of seizures is highly uniform within specific strains (*1–5*), so that animals with known susceptibilities can be selected for experiments. The incidence of otitis media, which may be a complicating factor in rats (*6–8*), is very low (*9, 10*). The types of seizures and stages in their genesis have been described (*4, 11, 12*). Apparatus has been developed for the control of the stimulus situation (*4, 13*), so that duplication of this factor is assured. And, finally, mice require much less space for rearing than do rats.

A serious objection to the use of mice as test animals in these studies, however, has been that they die in clonic-tonic seizures (*1, 3–5, 10*). To overcome this difficulty and, at the same time, to reduce the variability in response of individual mice at specific ages (*4*), we have had in progress for over two years a program of selection and progeny-testing of mice for specific susceptibilities to audiogenic seizures. The strains thus produced have been developed from an originally random albino stock and are variously inbred and outbred. All records of seizures are available from the start of the selection, because no mice have been saved for breeding without routine testing. As these strains may prove of value to other research workers interested in this aspect of rodent physiology and psychology, the characteristics of the strains that have been produced are briefly described herein. Breeding pairs of any of these strains of mice will be supplied to interested individuals for testing on request, within the limits of our resources.

Mice of the first strain, when tested daily from 15 to 50 days of age, have a very high incidence (90–100%) of clonic-tonic seizures, but they rarely die in the seizures. In the original stock there was one death for every 1.5 clonic-tonic seizures. At present there is only one death in approximately 250 seizures. This figure is by no means the maximum, because the testing of mice for breeding is routinely discontinued at

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50 days of age, when they are still highly susceptible. These animals continue to have seizures after that, if they are tested.

Mice of the second strain, when tested daily from 15 to 50 days of age, also have a high level of incidence of seizures, but the seizures are of the clonic type only. In this case, too, the mice do not die, because this type of seizure is rarely fatal (*11, 12*). In both these strains the latent periods of the seizures (i.e., the time elapsing between the start of the stimulus and the start of the seizure) are quite short (1–10 sec; av 5.3 ± 1.3 sec). In the original stocks the average latent period was 35 ± 2 sec. Thus testing is greatly expedited in these strains. The reduction in the latent period is probably the result of the increased susceptibility to seizures (*14, 15*).

Mice of the third strain, when tested from 15 to 50 days of age, have seizures at the 90–100% level between 17 and 24 days of age, but have 0–5% seizures between 30 and 50 days of age. These animals are valuable particularly in maturation studies, because the same animal is susceptible at one age and nonsusceptible only a few days later.

Mice of the fourth strain—by far the most difficult to produce—when tested similarly, have a very low incidence (5–10%) of seizures and have a large number of individuals that have no seizures at all. In the 22 offspring of one pair of these mice, for instance, 16 of the animals had no seizures. These nonsusceptible mice are valuable for comparison with the highly susceptible mice and for use in studies in which seizures are undesirable.

Details of the selection procedures and development of these strains will be presented elsewhere.

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A Metabolic Cage

THE Krebs tricarboxylic acid cycle is frequently referred to as a "furnace" in which intermediates are oxidized to CO_2 and H_2O. The initiated, who know enough not to take such statements literally, automatically include the subsequent electron transfer reactions, in which the ultimate acceptor is oxygen, as part of the system. Many students, however, have difficulty in understanding the relations of the two sets of reactions. As a means of demonstrating these relationships more clearly, the author has constructed a model (Fig. 1).

FIG. 1.

The reactions of the tricarboxylic acid cycle are represented as proceeding in a clockwise direction. Nonoxidative reactions are indicated by white arrows pasted flat to the base. Oxidation reactions in the cycle are indicated by raised red arrows which symbolize the loss of electrons. The transfer of electrons to the pyridine nucleotides is indicated by blue arrows, which are bowed toward the base. The series of electron transfers from the pyridine nucleotides, to the flavins, cytochromes, and finally to oxygen, is represented by the ascending groups of cards, each set with its red and blue arrows to indicate the electron transfers. One such group, starting with the isocitrate-oxalsuccinate: TPN-TPNH couple, faces the camera. Another series, beginning with the malate-oxalacetate: DPN-DPNH reaction, is shown from the rear. These two series illustrate the relationship adequately; hence the others have not been completed on the model. Blank cards are placed over the succinate-fumarate arrow as an admission that we do not as yet know all the answers.

To avoid confusion, many reactions and other details have been omitted. Thus, the transamination reactions, linkage with glycolysis, fatty acids, etc., could easily be added if desired. Likwise metals, cocarboxylase, phosphate, adenylic nucleotides, etc., are not depicted. Once a student grasps the central ideas, he has little difficulty adding these details to the conceptual superstructure. The cage does bring out the

sources of CO_2 and H_2O and the role of oxygen in respiratory reactions.

This particular model was constructed from a conic projection obtained from war surplus. Other cages could readily be constructed from the wire baskets obtainable at nurseries.

SHERMAN R. DICKMAN[1]

Department of Biological Chemistry
University of Utah College of Medicine
Salt Lake City

[1] The author wishes to acknowledge the aid of John Kemp in the construction of the model.

Sensitivity of Male dba Mice to the Toxicity of Chloroform as a Laboratory Hazard

FIFTY mice were sacrificed in this laboratory in a closed vessel containing some gauze soaked in chloroform. In the room in which the mice were killed 55 male dba mice were housed; within 6 days all but 5 of these mice were dead or dying. Autopsy disclosed large, pale, swollen kidneys, which were seen microscopically to have gross tubular necrosis. A considerable number of mice of strains A, C, C3H, and CAF1 hybrid, of both sexes, and 55 female dba mice remained quite healthy, although kept on the same rack and under the same conditions as the male dba mice.

The renal changes observed were similar to those reported by Eschenbrenner and Miller (*1*), who also noted that in strain A mice the males were more susceptible than the females to chloroform poisoning.

To confirm that the death of the male dba mice was indeed due to chloroform poisoning, 6 dba mice of each sex were placed near a beaker containing 5 ml of chloroform for 30 min. After 8 days 3 of 6 males were dead, and all had lesions resembling those seen in the original group. The female mice showed slight fatty degeneration of the liver but were otherwise well.

It would appear, therefore, that the male dba mouse is sensitive to the toxic effects of chloroform to such a degree as to constitute an unusual laboratory hazard.

PHILIPPE SHUBIK
A. C. RITCHIE
Division of Oncology, The Chicago Medical School

Reference

1. ESCHENBRENNER, A. B., and MILLER, E. *Science*, **103**, 302 (1945).

Book Reviews

Pharmacology in Clinical Practice. Harry Beckman. Philadelphia–London: Saunders, 1952. 839 pp. Illus. $12.50.

This book supersedes the author's *Treatment in General Practice*—a text which has seen six editions over a period of 22 years, the last edition appearing in 1948. Like the older one, the new book is oriented not about various classifications of drugs, but about diseases and other clinical situations that call for the use of drugs, as encountered in internal medicine and in the other medical and surgical specialties, as well as in dentistry.

In many instances, the disease or clinical situation is introduced by a concise paragraph highlighting the clinical problem. The drugs employed in treatment are then recorded, and their administration, clinical effects, absorption, excretion, and toxicity are described. Emphasis is on the practical use of these agents, rather than on their chemical and physical properties, which have been relegated to a separate section that includes some representative commercially available preparations. To conserve space, consideration of the historical development of drugs and of the relationship between chemical structure and biologic activity has been omitted, and consideration of the mechanism of drug action has been abbreviated.

Many of the more recent developments in therapy are presented, including the use of synthetic curare substitutes, newer antibiotics, isonicotinic acid hydrazides, stilbamidine (for some mycotic diseases), autonomic blocking agents, ion exchange resins and N-allyl-normorphine. The author demonstrates a good sense of proportion in his consideration of new drugs, as well as in his evaluation of the usefulness of ACTH and cortisone, and of anticoagulants. Drugs which are unproved or subject to conflicting claims are so described. Where any one of several agents may be utilized, the author frequently indicates which, in his opinion, is superior.

Although these opinions are, in the main, reasoned and sound in the light of current practice, it is unfortunate that the author has not provided better documentation and more references than are listed in the "suggested excursions into the literature." This would put in proper perspective a few of the author's comments that are open to question—for example, that "coronary disease is not a contraindication to dihydroergocornine's use" (in hypertension), that "tolerance to hexamethonium has not been demonstrated," that "many experienced men strongly oppose intravenous administration of any fluid in cases of massive hemorrhage" (from peptic ulcer), and that "atropine should always be at hand . . . but should never be injected with the prostigmin" (in the diagnostic test for myasthenia gravis). Statements such as these are few, however. The great majority of recommendations concerning therapy are in accord with sound current practice, so that this book, which is written in a clear

and interesting manner, should be useful in introducing students of medicine, dentistry, and allied professions to the current clinical use of drugs, and in summarizing for physicians many of the newer developments.

DAVID GROB

Department of Medicine
Johns Hopkins University School of Medicine

Filter Design Data for Communications Engineers. J. H. Mole. New York: Wiley, 1952. 252 pp. Illus. $7.50.

In Dr. Mole's words, "Existing textbooks on filters concentrate on theoretical principles and give comparatively little attention to the needs of the practical designer; the present work is an attempt to supplement them by providing in a convenient form charts, tables and formulae which have been selected or constructed so as to lighten the labour of calculation as much as possible." In brief, this is a designer's handbook covering calculations of low-pass, high-pass, band-pass, and band-stop filters. The calculations are for the most part based on the approximations of Campbell and Zobel. An approximation based on the assumption that the frequency response follows "Tchebycheff behavior," is also included. The following functions are tabulated: (1) reciprocals and squares of $\omega = 2\pi f$, (2) hyperbolic and exponential functions, (3) functions $\sqrt{1-x^2}$, $\frac{1}{x} - x$ and their reciprocals.

BEN GOSSICK

Department of Physics, Purdue University

Thermochemical Methods in Silicate Investigation. Wilhelm Eitel. New Brunswick, N. J.: Rutgers Univ. Press, 1952. 132 pp. Illus. $4.75.

In this book—small in the sense that there are few pages—the author has attempted to combine descriptions of the instruments used in this country and abroad, for calorimetric measurement of the heat effects accompanying transformations involving silicates and related materials, with a discussion of the use of the data obtained with these instruments for the calculation of useful thermodynamic functions.

After brief introductory statements, the first section deals in a clear, almost elementary way with the determination of heats of formation and reaction by the use of Kopp's law, with due emphasis on the caution with which such methods must be used.

Next is a section which describes a selection of the various calorimeters that have been used to determine heats of reaction. The descriptions are necessarily brief, but some important details of construction are given, as well as minimal discussion of the errors. There is also a brief treatment of some of the attempts by various authors to calculate heats of reaction from structural data and fundamental physical constants.

The remainder of the book is concerned, for the most part, with the problem of reaction affinities. The general principles which relate the driving forces that bring about silicate reactions to entropy and free energy are considered.

Calorimeters for the measurement of both low and high temperature heat capacities are described. The use of low temperature heat-capacity data and the third law to calculate numerical values for the entropy and free energy changes is described and illustrated in a clear and practical manner. Instances of the successful application of these methods to stability problems involving minerals are cited, and hope is expressed that they will prove to be of use in the study of problems related to rock formation and mineral paragenesis as the volume and quality of thermochemical data are increased.

Appendix I deals with practical evaluation of the results of calorimetric determination. Two examples with data and complete calculations, including temperature corrections, are given. Appendix II consists of tables of data from the literature.

There are a few errors not detected in the proofreading, but these are minor.

The author has used the terms "crystalline solution" and "structure energy" throughout the book. Although no objection can be offered to these terms, it may be that most readers in this country feel more at home with "solid solution" and "lattice energy," and in consequence these will continue to be used by the majority of workers.

The international reputation of the author and his long and varied experience in silicate chemistry eminently fit him to write such a book. The German influence is apparent in the style of the presentation. Nevertheless, this is a clear and readable book which will be valuable to those interested in the practical problems of experimental work on the thermochemistry of silicate and allied materials.

J. S. MACHIN

Geochemical Section
Illinois State Geological Survey, Urbana

Scientific Book Register

Archeology of Eastern United States. James B. Griffin, Ed. Chicago: Univ. of Chicago Press; London: Cambridge Univ. Press, 1952. 392 pp. and plates. $10.00.

Electromagnetics. John D. Kraus. New York–London: McGraw-Hill, 1953. 604 pp. Illus. $9.00.

Two Roads to Truth: A Basis for Unity under the Great Tradition. Edmund W. Sinnott. New York: Viking Press, 1953. 241 pp. $3.50.

Understanding the Weather. Revision of *Knowing the Weather.* T. Morris Longstreth. New York: Macmillan, 1953. 118 pp. and plates. $2.50.

The Riddle of Cancer. Rev. ed. Charles Oberling; trans. by William H. Woglom. New Haven: Yale Univ. Press; London: Geoffrey Cumberlege, Oxford Univ. Press, 1952. 238 pp. $5.00.

The Radiant Universe. George W. Hill. New York: Philosophical Library, 1952. 489 pp. Illus. $4.75.

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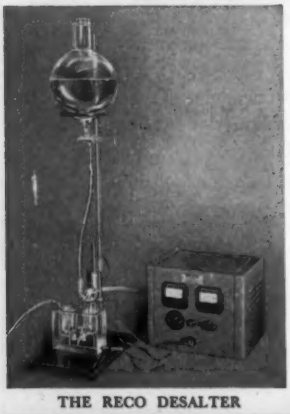

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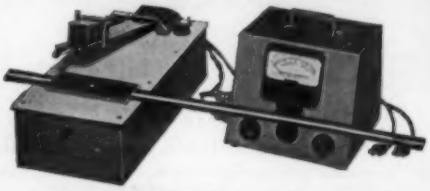

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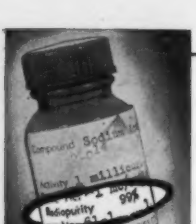

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Mar. 20–22. International Association for Dental Research (Annual). Ben Franklin Hotel, Philadelphia.
Mar. 22–25. American Association of Dental Schools. Ben Franklin Hotel, Philadelphia.
Mar. 23–25. American Congress on Surveying and Mapping (Annual). Hotel Shoreham, Washington, D. C.
Mar. 23–25. Conference on Placement of Severely Handicapped. Washington, D. C.
Mar. 23–26. American Association of Petroleum Geologists, Society of Economic Paleontologists and Mineralogists, and Society of Exploration Geophysicists (Joint Annual). Coliseum, Houston.
Mar. 23–26. Institute of Radio Engineers (Annual). Waldorf-Astoria Hotel and Grand Central Palace, New York.
Mar. 23–27. Conference on Tropical Architecture. University of London, England.
Mar. 23–27. Western Metal Congress and Exposition. Pan-Pacific Auditorium, Los Angeles.
Mar. 25–27. American Association of Anatomists (Annual). Ohio State University, Columbus.
Mar. 25–27. American Power Conference (Annual). Sherman Hotel, Chicago.
Mar. 26–27. Chemical Society Anniversary Meetings. London.
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Mar. 26–28. American Physical Society. Durham and Chapel Hill, N. C.
Mar. 26–28. Eastern Colleges Science Conference. New York State College for Teachers, Albany.
Mar. 27. Association for Research in Ophthalmology, Midwestern Section. Oscar Johnson Institute, St. Louis.
Mar. 29–Apr. 1. Society of German Chemists, Union of Austrian Chemists, and Swiss Chemical Society (Chemical Meeting). Innsbruck.
Mar. 30–31. Symposium on Retinal Diseases. Department of Ophthalmology, College of Medicine, State University of Iowa, Iowa City.
Mar. 30–Apr. 2. Association of American Geographers (Annual). Cleveland.
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Apr. 6–10. American Physiological Society (Spring). Chicago.
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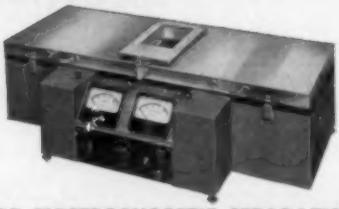

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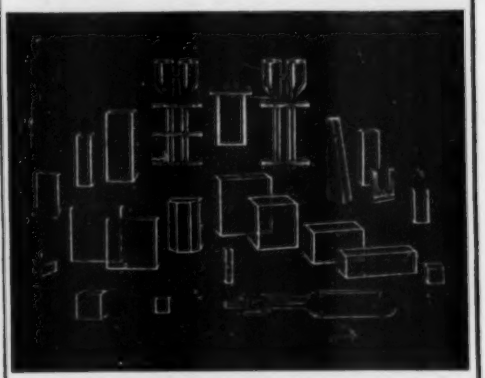

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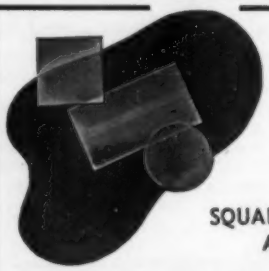

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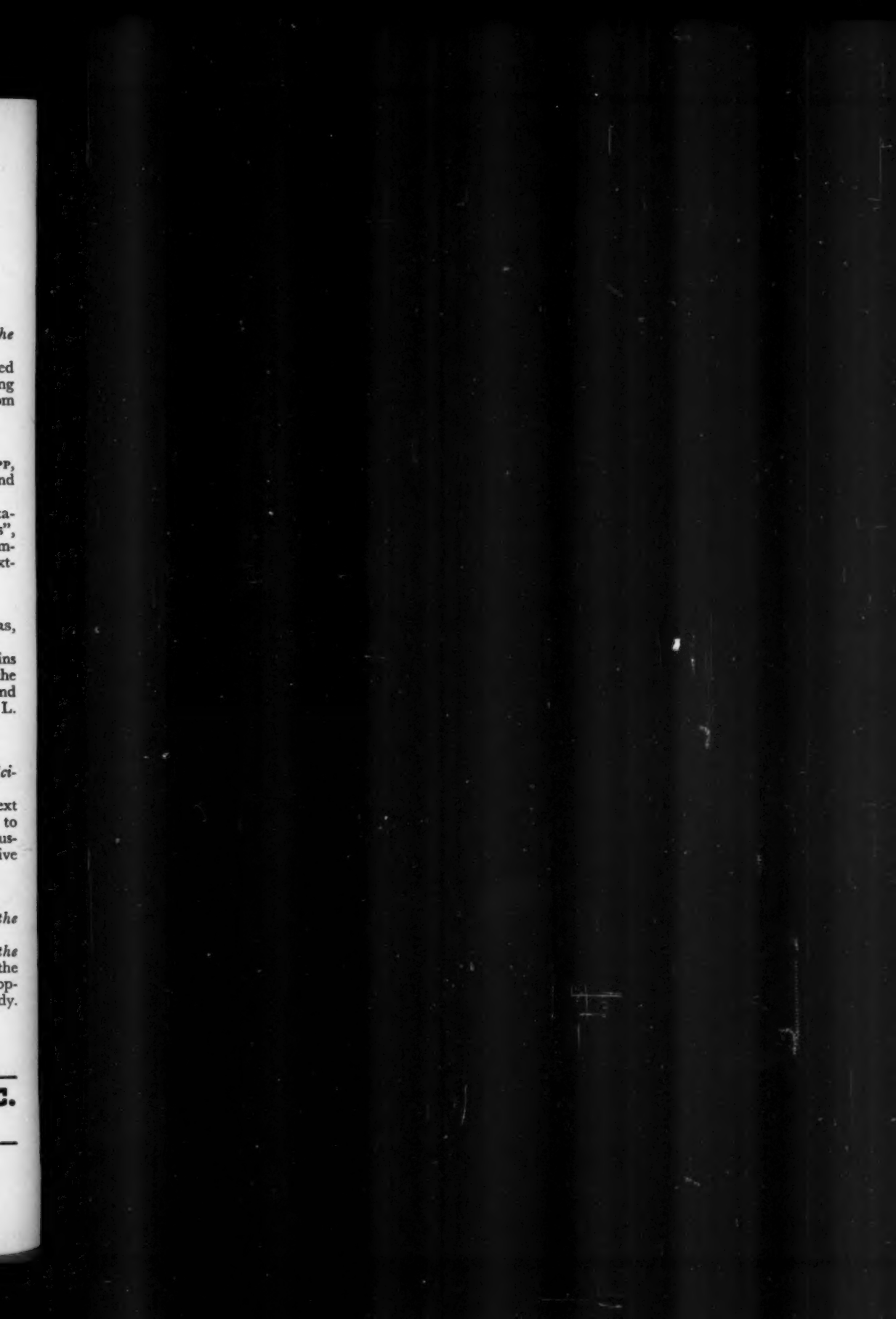
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